MEDICAL STATE BOARD

QUESTIONS and ANSWERS

FLIPPIN

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Tenth Edition

MEDICAL STATE BOARD

QUESTIONS and ANSWERS

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/SID Sci – USID Sci, TPK

to

PATRICK HENRY CALLAWAY

with appreciation

PREFACE TO THE TENTH EDITION

The main objective that guided the writing of the first edition of this book fifty-five years ago has also served in the preparation of the tenth edition. This objective is to present to the student of medicine reliable, up-to-date medical information in convenient, concise, yet adequate form.

This edition reflects the many strides which have been made in medicine during the past five years. Without attempting an all-inclusive list, mention may be made of a few, namely, newly recognized diseases (pulmonary alveolar proteinosis, adenoviral, ECHO, and respiratory syncytial viral infections and others); new antimicrobial agents ("long-acting" sulfonamides, "synthetic" penicillins, vancomycin, amphotericin B, griseofulvin, and others); additional data concerning poliomyelitis vaccines (Salk and Sabin); oral compounds for the control of diabetes mellitus (aryl sulfonylureas); better oral diuretics (thiazide derivatives); improved adrenal glucocorticoids (dexamethasone, etc.); the introduction of extracorporeal hemodialysis; a better understanding of the selection of patients for cardiac surgical procedures; additional experience with long-term anticoagulant therapy; new techniques for the transplantation of tissues and improvement in synthetic prostheses; additional information pertaining to problems related to ionizing radiation, and data concerning disorders associated with travel.

In the present edition all chapters received attention and required some change. Several parts have been rewritten and some subjects enlarged as seemed advisable because of relative importance, current interest and recent new information. Special emphasis has been given to preparation of the index, which should enhance the usefulness of the book.

It is with regret that the editor reports the deaths of two editorial consultants, Jefferson H. Clark, M.D. and George M. Eisenberg, Sc.D. The editor wishes to express his thanks to the members of the editorial board, whose important contributions made the revision of this book possible, to A. L. Halpern, M.D. for his detailed review of the ninth edition for typographical errors, and to the publishers for their consideration and helpful guidance.

Harrison F. Flippin

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Section 1

ANATOMY

CIRCULATORY SYSTEM

The Heart

✓ **Give a brief yet comprehensive description of the heart.**

The heart is a hollow muscular pump surrounded by the pericardium. It contains four cavities: a right and left atrium and a right and left ventricle. The right atrium receives blood from the superior and inferior venae cavae and transmits it through the tricuspid valve opening into the right ventricle. Part of the right atrium is like the large veins in structure and is called the sinus. Each atrium has a small appendage, the auricle. On the septum between the right atrium and the left atrium lies the limbus ovalis, which surrounds the fossa ovalis. The fossa is the remnant of the foramen joining the right and left atrium in fetal life. There is a small fold of membrane at the opening of the inferior cava called the valve of the vena cava (Eustachian). The coronary sinus bringing blood from the heart wall empties at this location. The pulmonary artery, which has semilunar valves at its mouth, leaves the right ventricle at the pulmonary conus. The tricuspid valve leaflets are attached to the papillary muscles of the ventricle wall by the chorda tendinea.

The left atrium receives the blood returning from the lungs and passes it through the bicuspid valve (mitral) to the left ventricle. The left ventricle is smaller than the right, but the wall is thicker, and the papillary muscles are much larger. The blood is pumped from the left ventricle into the aorta, which has at its orifice three similunar valves. The coronary arteries arise from behind two of these cusps and supply arterial blood to the heart. The coronary veins return the blood. The nerve supply is from the vagus nerve and from the cardiac plexus of the sympathetic.

The heart muscle is a special form of striated muscle. The muscle of the atrium does not continue with the muscle of the ventricles but stops at the annulus fibrosus. The ventricular muscle begins at the annulus fibrosus and is oriented in a special pattern. The outer layer of the muscle forms a helix that goes around both ventricles. The deeper layers surround each ventricle and in the interventricular septum cross over like a figure of eight to the ventricle of the other side. Each ventricle has a set of fibers belonging wholly to it. These begin at the annulus and proceed around the ventricle as a helix until they reach the apex of the ventricle. Here they weave into the interior of the ventricle and turn upward to be continued as the papillary muscles. The chorda tendinea continues from here to the valve flaps, which in turn are attached to the annulus fibrosus, thus furnishing the second point of attachment of the heart muscle and making of the ventricle a contractible chamber.

Locate and describe the pericardium.

A pyramidal, fibroserous sac surrounding the heart and great vessels, the base attached to the central tendon of the diaphragm, the apex corresponding to the great vessels at the base of the heart and connected with the deep cervical fascia by fibrous prolongations. It is placed behind the sternum and the cartilages of the fourth, fifth, and sixth ribs of the left side, in the interval between the pleurae. The inner, serofibrous layer forms a closed sac that covers the heart and great vessels and sometimes contains a small quantity of fluid—the *liquor pericardii.*

Arterial supply from *internal mammary* artery and *descending aorta.* Nerves: *phrenic, sympathetic* and *tenth.*

Describe the endocardium.

A thin membrane lining the internal surface of the heart. It assists in forming the valves by its reduplications and is continuous with the intima of the vessels. It is smooth and transparent and covered with a single layer of *endothelial cells.*

What is the atrioventricular bundle (of His)?

A bundle of conducting tissue, 2 mm. broad and 1 mm. thick, begins at the atrioventricular node in the lower part of the interatrial septum and passes into the interventricular septum at the membranous part where it divides into right and left branches that arborize throughout the myocardium.

The sinoatrial node is related to this complex but not directly connected with it. It is the pathway by which the impulse initiating the contraction of the heart is conveyed from the atrium to the ventricle.

Beneath what points on the anterior surface of the chest are the cardiac valves?

Pulmonary: To the left of the upper part of the third left chondrosternal junction.

Aortic: Behind left half of sternum, opposite lower border of third costal cartilage.

Bicuspid (*Mitral*): Behind left half of sternum, opposite fourth rib.

Tricuspid: Opposite middle of sternum, at the level of the fourth and fifth cartilages.

What are the special characteristics of the left ventricle of the heart?

It forms the apex of the heart and contains the aortic opening. Its walls are thicker than those of the right ventricle. Its papillary muscles are fewer and larger. The atrioventricular (mitral) valve is made up of two segments.

What arteries supply the heart with blood, and where do they originate?

The two coronary arteries springing from the ascending aorta: the right from the *right* (*anterior*) *aortic sinus* (sinus of Valsalva); the left from the *left* (*anterior*) *aortic sinus.*

Where is the foramen ovale of the heart and what purpose does it serve?

In the wall between the atria. In the fetus it permits the passage of blood from the right to the left atrium, and carries the blood which enters the right atrium from the inferior vena cava to the left atrium, thereby saving the pulmonary circulation from engorgement.

Describe the changes that take place in the vascular system at birth.

The blood ceases to flow through the *umbilical vein* and *ductus venosus* into the inferior cava; the *umbilical arteries* become obliterated after ligation of the umbilical cord. The foramen ovale no longer serves to balance the circulation and gradually closes. The *ductus arteriosus,* which connects the pulmonary artery with the arch of the aorta, is functionally useless when the pulmonary circulation is established with the first breath and is slowly obliterated.

The Arteries

Describe the structure of the arteries and give their nerve and blood supply.

✓

Arteries have three coats or tunicae. The inner endothelial layer, the intima, has a basement membrane of elastic tissue. The next layer, the media, consists of smooth muscle fibers in a circular arrangement. The outer layer, the externa, is the connective tissue layer that is the sheath of the artery. When an artery is surgically clean this layer has been removed. A plexus of unmedullated nerve fibers is found in the externa. These come from sympathetic ganglia and are basically motor nerves. A few unmedullated nerves, afferent in function, are found in the larger arteries. Vessels over a millimeter in diameter have vasa vasorum. In the tunica externa, these arise from the artery and supply the wall except the intima. The returning veins empty into adjacent veins.

What is the circulus arteriosus?

The circulus arteriosus (circle of Willis) is an arterial anastomosis on the base of the brain. It begins behind with the two terminal branches of the basilar, the posterior cerebrals. The posterior communicating arteries join these with the internal carotid arteries. The anterior part is continued by the two anterior cerebrals which leave the carotids. The most anterior link is the anterior communicating artery.

What arteries unite to form the basilar artery?

The two vertebrals.

Give the origin, distribution, and branches of the middle meningeal artery.

It is a branch of the internal maxillary artery, which enters the cranium through the foramen spinosum. Its branches course upward and backward in the dura mater in two groups, anterior and posterior. At the anterior end of the middle cranial fossa, it usually has a short intraosseous course. This is the section commonly ruptured in skull fracture. The ultimate distribution is to the dura mater and especially the vault of the skull. There is generally a small separate artery, the anterior meningeal artery, in the anterior cranial fossa, and a small posterior meningeal artery in the posterior cranial fossa.

Give the origin and course of the pulmonary artery.

The pulmonary artery is the most anterior artery of the heart. It arises from the pulmonary conus of the right ventricle. It ascends to the left of the aorta and, curving under the arch, divides at this point into the right and left pulmonary arteries. This is on a line with the angle of the sternum in front and the fifth vertebra behind.

What blood vessels pass to and from the liver?

The arteria hepatica propria ascends to the liver through the hepatoduodenal ligament. In addition, the vena porta also enters from below. A series of large and small hepatic veins drain the liver directly into the inferior vena cava.

Describe the external carotid artery.

It arises opposite the upper border of the thyroid cartilage and then slopes backward to the space between the mandible and the external auditory canal, where it divides into the superficial temporal and the internal maxillary. On its upward course it gives off the superior thyroid, lingual, external maxillary, occipital, posterior auricular, and ascending pharyngeal arteries.

Name the branches of the subclavian artery.

Although the left subclavian coming from the arch of the aorta is longer than the right, which comes from the innominate, the branches are similar. They are the vertebral, internal mammary, superior intercostal, thyrocervical trunk, inferior thyroid, transverse cervical, and transverse scapular. The subclavian artery at the outer border of the first rib becomes the axillary artery.

Through what arteries is the collateral circulation carried on after ligation of the subclavian artery?

After ligation of the third part of the subclavian (site of election), the circulation is maintained chiefly by *three* sets of vessels: a *posterior* set, consisting of the transverse scapular and posterior scapular branches of the subclavian, anastomosing with the subscapular branch of the axillary; an *internal* set, consisting of the internal mammary, anastomosing with the superior and long thoracic and subscapular branches of the axillary; a *middle* set, consisting of small branches of the subclavian anastomosing with branches of the axillary artery.

Give the origin, main branches, and relations of any one of the following arteries: external carotid, axillary, and femoral.

The *axillary artery* is the continuation of the subclavian and becomes the brachial artery. It extends from the outer border of the first rib to the lower border of the teres major, where it becomes the *brachial artery.* It is divided into *three* portions by the pectoralis minor: First portion: *in front,* pectoralis major, costocoracoid membrane; *outer side,* brachial plexus; *inner side,* axillary vein; *behind,* ribs and intercostal muscles. Second portion: *in front,* pectoralis minor; *outer side,* outer cord; *inner side,* inner cord; *posteriorly,* posterior cord and subscapularis muscle. Third portion: *in front,* pectoralis major; *outer side,* coracobrachialis muscle and median and musculocutaneous nerves; *inner side,* ulnar and medial cutaneous nerves and axillary vein; *behind,* subscapularis, latissimus dorsi, and teres major muscles and radial and axillary (circumflex) nerves.

Branches: Supreme thoracic, thoracoscapular; and anterior and posterior ciracromial, lateral and alar thoracic; subcumflex.

Give the origin, course, and branches of any one of the following arteries: brachial, temporal, and left common carotid.

The *brachial* commences at the lower margin of the tendon of the teres major and passes down the inner and anterior aspects of the arm, terminating about ½ inch below the bend of the elbow, where it divides into the radial and ulnar arteries. Its *branches* are: the profunda artery of the arm, muscular and nutrient branches, superior ulnar collateral, and inferior ulnar collateral.

What would be the collateral circulation if the brachial artery were ligated below the profunda artery of the arm?

The profunda and superior ulnar collateral anastomose with the inferior ulnar collateral, the radial and interosseous recurrent, and the volar and dorsal ulnar recurrent.

✓ **Describe the location of the intercostal arteries.**

They are located below the subcostal grooves on the under surface of the ribs.

What arteries, muscles, and nerves would be severed in a cross section at the middle of the humerus?

The brachial, profunda, and superior ulnar collateral arteries; the biceps and triceps muscles, the insertion of the deltoid, the coracobrachialis, and the origin of the brachialis muscles; the musculocutaneous, medial cutaneous of the forearm, median, ulnar, and radial nerves.

Describe the ulnar artery as to (a) origin, (b) course, and (c) distribution.

(*a*) It is the larger terminal branch of the brachial and commences in the cubital fossa, terminating in the palm.

(*b*) From its origin it runs obliquely downward and inward, beneath the muscles arising from the medial epicondyle to the junction of the proximal and middle thirds of the forearm. From that point it descends to the wrist, passing to the radial side of the pisiform bone, and forms the *superficial volar* arch. (*c*) The ulnar artery supplies the structures on the inner side of the elbow, the ulnar side of forearm and wrist, the interosseous membrane and adjacent muscles, and also flexor surface of the hand.

In amputation of the forearm 3 inches above the wrist, what arteries will it be necessary to tie, and of what are they branches?

Radial and ulnar arteries, branches of the brachial; volar and dorsal interosseous arteries, branches of the ulnar.

Describe the position of the volar arterial arches.

The *superficial volar arch* lies upon the flexor tendons and passes across the palm at the level of the medial border of the thumb when in extreme abduction. The *deep volar arch* lies upon the metacarpal bones and interossei muscles, ½ inch nearer the carpus than the superficial arch.

Name the branches of the abdominal aorta.

Visceral: Celiac axis, superior mesenteric, inferior mesenteric (unpaired); suprarenal, renal, testicular or ovarian (paired).

Parietal: Middle sacral (unpaired); inferior phrenic, lumbar (four pairs), common iliac (paired).

Mention the principal branches of the celiac axis.

Left gastric, hepatic, and splenic arteries.

✓ **Where does the abdominal aorta commence and where does it terminate?**

It commences at aortic opening in diaphragm, on body of twelfth thoracic vertebra; terminates on body of fourth lumbar vertebra, just to left of median line.

Mention the branches of the hypogastric (internal iliac) artery.

Anterior Trunk: Superior, middle, and inferior vesical, obturator, middle hemorrhoidal, uterine, vaginal, internal pudendal, and inferior gluteal.

Posterior Trunk: Iliolumbar, superior gluteal, and lateral sacral.

What arteries supply the bladder in the male? Of what vessel are they branches?

Superior, middle, and inferior vesical; branches of hypogastric.

Describe the relation of the deep (inferior) epigastric artery to the abdominal inguinal (internal abdominal) ring.

The artery descends to reach the inguinal (Poupart's) ligament, then ascends obliquely along the medial margin of the abdominal inguinal ring and passes upward in the abdominal wall, between the transversalis fascia and the peritoneum.

Describe the femoral artery and its branches.

The femoral artery is the continuation of the external iliac. Commencing immediately behind the *inguinal ligament,* midway between the anterior superior spine and the symphysis, it passes down the thigh and terminates at the opening in the adductor magnus muscle. The proximal portion lies in the *femoral trigone* (Scarpa's triangle) and is superficial; at the apex of the trigone it passes to the sartorius muscle and enters the adductor (Hunter's) canal, becoming more deeply placed.

Branches: Superficial circumflex iliac, superficial epigastric, superficial external pudendal; muscular, deep external pudendal, profunda femoris, and arteria genu suprema (anastomotica magna).

The *profunda artery* (profunda femoris) is the largest branch of the femoral artery. It arises 1½ inches below the inguinal ligament; curving backward, it passes posterior to the femoral artery and runs distally along the medial side of the femur to the back of the thigh, after perforating the adductor magnus muscle.

Branches: Three perforating arteries: lateral and medial circumflex arteries, arteria genu suprema. Terminates as the fourth perforating artery.

Describe the femoral sheath.

A funnel-shaped sheath formed by the transverse fascia anteriorly and the iliac fascia posteriorly, which surrounds the femoral artery and vein at their entrance into the *femoral trigone.* The three compartments into which it is divided by anteroposterior septa contain the following structures:

The *lateral compartment* is comprised of the femoral artery and the lumboinguinal branch of the genitofemoral nerve.

The *medial compartment* constitutes the femoral canal. The medial wall is pierced by great saphenous vein.

The *intermediate compartment* comprises the femoral vein.

If the femoral artery were obstructed at the apex of the femoral triangle, through what channels would the blood flow to reach the tibial arteries?

The new channels would be formed by the profunda and its branches. The lateral circumflex anastomoses with the arteria genu suprema, the medial circumflex with the superior articular, and both anastomose with muscular branches. The arteria comitans nervi ischiadici branch of the inferior gluteal anastomoses with branches from the popliteal and posterior tibial arteries.

Describe the popliteal artery and give its branches.

The popliteal artery is the direct continuation of the femoral. It begins at the proximal and medial part of the popliteal fossa and terminates at the distal border of the popliteus muscle, where it divides into the anterior and posterior tibial arteries. It lies upon the posterior surface of the femur, the posterior part of the capsule of the knee joint, tibia, and the fascia covering the posterior surface of the popliteus, bisecting the popliteal space longitudinally.

Branches: Proximal and distal (sural) muscular branches; superior and inferior lateral genicular (articular); superior and inferior medial genicular; middle genicular; anterior and posterior tibial.

Give the course of the posterior tibial artery.

It commences at the border of the popliteus muscle and terminates midway between the tip of the medial malleolus and the calcaneus. The artery runs downward and inward between the superficial and deep flexor muscles of the calf.

In an amputation of the leg 5 inches below the knee, what arteries will it be necessary to tie and of what are they branches?

Anterior and posterior tibial, branches of popliteal; peroneal artery, branch of posterior tibial.

The Veins

Describe the superior vena cava.

It returns the blood from the head, neck, upper extremities, thoracic wall, and a portion of the upper part of the posterior wall of the abdomen. It is formed behind the first right costal cartilage by the *union of the two innominate veins,* and descends, with a slight convexity to the right, to the level of the third right costal cartilage, where it opens into the upper and back part of the right atrium. The lower half is within the pericardium. Its *tributaries* are the vena azygos (vena azygos major), pericardial, and mediastinal veins.

Describe the inferior vena cava and name the veins that enter into its formation.

It returns the blood to the heart from practically all parts of the body below the diaphragm. It is formed by the *junction of the two common iliac veins* on the right side of the intervertebral disk between the fourth and fifth lumbar vertebrae. Passing upward on the front of the spine, where it lies to the right of the aorta, it traverses the under surface of the liver in the fissure of the vena cava, perforates the central tendon of the diaphragm at the level of the eighth thoracic vertebra, and enters the pericardium, terminating in the lower back part of the right atrium.

Describe the right and left subclavian veins.

The *subclavian vein* extends from the lower border of the first rib to a point behind the sternoclavicular articulation, where it unites with the internal jugular to form the innominate. The vein lies in front of the artery, separated from its second portion by the anterior scalene muscle. Its *tributaries* are the external and anterior jugular.

On the *right side* the right lymphatic duct empties into the subclavian vein at its junction with the internal jugular; the *left* subclavian vein receives the thoracic duct at this point; otherwise the course and relations of the vein are the same on the two sides.

Describe the internal jugular vein.

The vein is formed in the jugular foramen by the junction of the lateral and inferior petrosal sinuses. It comes down the neck, beneath the anterior border of the sternocleidomastoid muscle, accompanied first by the internal, and then by the common carotid artery, and throughout its course by the vagus (pneumogastric) nerve. The vein is contained *in the same sheath with the artery and nerve* but separated from these structures by a distinct septum. At first the vein lies behind the internal carotid artery; but as it descends it gradually passes to the other side of the vessel and later along the outer side of the common carotid, partially overlapping the artery in front, to its termination behind the sternoclavicular articulation, where it unites with the subclavian to form the innominate.

Give the course and relations of the external jugular vein.

The vein is formed on the surface of the sternocleidomastoid muscle, below the angle of the jaw, by the *union of the posterior auricular with a branch of the posterior facial* (temporomaxillary) vein. It descends to the anterior part of the subclavian portion of the posterior triangle of the neck and there terminates in the subclavian vein, after piercing the deep fascia and crossing the third portion of the subclavian artery.

Describe the portal system.

It is made up of veins that drain the spleen, stomach, pancreas, and large and small intestines. The *splenic vein,* after receiving the inferior mesenteric, joins the superior mesenteric to form the *portal vein,* which receives the *gastric.* The portal vein passes behind the hepatic artery and bile duct in the lesser omentum and enters the *porta hepatis* or *gate* (transverse fissure) *of the liver,* where it divides into minute branches.

How are the saphenous veins formed? Where do the saphenous veins empty?

The great (internal) is formed by the union of the medial extremity of the dorsal venous arch with the dorsal vein of the great toe; it empties into the femoral vein. The small (external) is formed by the union of the lateral extremity of the dorsal venous arch with the lateral dorsal vein of the little toe and empties into the popliteal vein.

Give a general description of the cerebral veins.

They are remarkable for the thinness of their walls, owing to lack of muscle tissue, and have no valves. The *superficial* cerebral veins are lodged in the sulci between convolutions; the veins receive blood from the substance of the brain and empty into the sinuses, pouring in their contents in a direction opposite to the current in the sinuses. The *deep* cerebral veins drain the ventricles into the straight sinus; the basal vein drains the interpeduncular space and the basal ganglia.

Lymphatic System

What is the lymphatic system? Describe the thoracic and right lymphatic ducts.

The lymphatic system consists of lymph ducts, nodes, and fluid lymph. The lymph ducts drain the lymphatic glands. They extend to every portion of the body. The ducts in the lower abdomen, and lower extremities unite to form the *cisterna* (receptaculum) *chyli.* This lymph space is drained by the *thoracic duct* which, after receiving the tributaries from the left half of the thorax, upper extremity, and head, empties into the left subclavian vein. The *right lymphatic duct* drains the right side of the head and thorax and the right upper extremity, and empties into the right subclavian vein.

Describe the thoracic duct.

It begins opposite the first and second lumbar vertebrae in a dilated pouch called the *cisterna chyli,* passes through the aortic opening in the diaphragm, and then, through the posterior and superior mediastinum, to the base of the neck, where it arches to the left and terminates at the *junction of the left subclavian and internal jugular veins.* It drains the lymph from all parts of the body except the right upper extremity, right side of the head and neck, right half of the thorax (right lung and right side of the heart), and upper surface of the liver.

What are the lymphatic nodes?

They are globular, ovoid, flattened bodies, consisting of fibrous framework, lymph sinuses, and lymph follicles. They form part of the general lymphatic system.

Give the situation of the lymphatic nodes of the chest.

Sternal (*internal mammary*): At the margin of the sternum along the line of the internal mammary artery.

Intercostal: Lateral in the posterior parts of the intercostal spaces; *medial* in front of the heads of the ribs.

Mediastinal: Anterior and posterior in the anterior and posterior mediastinal spaces. The anterior are divided into an upper and a lower group.

Bronchial: Along the trachea and main bronchi and their intrapulmonary branches.

Locate and describe the aggregated lymphatic nodules (Peyer's glands).

They are entirely confined to the *small intestine,* being largest and most numerous in the ileum, and situated opposite the attachment of the mesentery. The glands consist of a large number of *lymphoid nodules* grouped closely together so as to form a slightly elevated area, usually oval in form. Length from ½ inch to 3 inches; width from ⅓ to ½ inch.

GLANDS

Name and describe the salivary glands.

Parotid, submaxillary, and sublingual.

The *parotid gland* lies upon the side of the face, immediately below and in front of the ear, limited above by the zygoma. It empties its secretion into the mouth by way of the *parotid* (Stensen's) *duct,* which runs parallel with the zygoma and pierces the buccinator muscle and the mucous membrane of the cheek opposite the second upper molar tooth.

The *submaxillary gland* is below the jaw in the submaxillary triangle; it is irregular in form and weighs about ⅛ ounce. The *submaxillary* (Wharton's *duct* is about 2 inches long. It passes forward and inward and opens by the side of the frenum of the tongue.

The *sublingual gland* is situated beneath the mucous membrane of the floor of the mouth by the side of the frenulum, in contact with the inner surface of the mandible. The *ductus sublin-*

guales minores (ducts of Rivinus), eight to twenty in number, open on the floor of the mouth on each side of the frenulum; one larger duct opens into the submaxillary duct and is called the *ductus sublingualis major* (duct of Bartholin).

Structure: The salivary glands are compound racemose glands, consisting of numerous lobules, each one having a single duct, which terminates in an alveolus. The glands are of two kinds: one secretes mucin, the other serum albumin. The sublingual gland is an example of the first variety, the parotid, of the second, while the submaxillary gland represents a combination of both varieties.

Give the course and relations of the parotid duct.

Stensen's duct is formed in the parotid gland, crosses the masseter muscle a fingerbreadth below the zygoma, and perforates the buccinator muscle and the mucous membrane of the cheek opposite the second upper molar tooth.

Give the point of opening of the parotid duct, of the submaxillary duct, and of the sublingual duct.

The *parotid* duct opens in the cheek wall opposite the second upper molar tooth; the *submaxillary* duct opens in the mouth at the tip of the frenulum linguae; the *sublingual* ducts open on the floor of the mouth by the side of the frenulum linguae.

Locate and describe the lacrimal glands.

Lodged in a depression in the superior and lateral part of the orbital cavity, the lacrimal gland is about the size and shape of an almond. It consists of two portions—the *superior* and *inferior* lacrimal glands. The superior, much the larger, occupies the *lacrimal fossa* on the medial surface of the zygomatic process of the frontal bone. The smaller, inferior gland lies below and in front of the superior (*orbital portion*), and is in contact with the upper eyelid and the conjunctiva. The two portions are separated by the expansion of the tendon of the levator palpebrae superioris muscle.

The vessels and nerves enter the gland at its posterior border.

The *structure* is that of a compound racemose gland resembling the parotid. The secretion is *serous* and is poured out on the conjunctiva by seven or eight ducts at the upper and lateral sides of the palpebral angle.

Describe the glandulae tarsales (meibomian) glands.

They are *sebaceous* glands, each consisting of a straight follicle, with numerous small secondary follicles opening into it. There are about 30 in number on the upper and 25 on the lower lid, occupying the inner surface of the eyelids, between the tarsal plate and the conjunctiva. The ducts open on the free margin of the lids. The secretion prevents adhesion of the lids.

Describe the mammary glands.

They are accessory glands of the generative system, which *secrete milk* in the female but exist only in a rudimentary state in the male. In the female the mammae appear as two hemispheric glands on the front of the chest, between the third and the sixth ribs, and extend from the edge of the sternum to the anterior axillary fold. They consist of 10 to 16 *racemose* glands held together by fibrous and fatty tissue. Each lobule consists of a cluster of alveoli and is provided with a single, small duct, which expands into an ampulla before terminating at the apex of the *nipple*. There are 15 or 20 of these *lactiferous ducts*. The nipple is a conical eminence surmounting the gland and surrounded by a pigmented areola that contains small glands.

Name the endocrine glands.

Pineal, pituitary, thyroid, parathyroid, thymus, adrenals, para-aortic bodies, carotid and coccygeal glomera, and parts of liver, pancreas, testis, and ovary.

Describe the thyroid gland.

The *thyroid* is a ductless gland. When fully developed it consists of two lateral *lobes,* conical in form, situated on the sides of the upper portion of the trachea and alae of the thyroid cartilages. The lobes are connected by a narrow transverse *isthmus.* At times a third lobe is found springing from the isthmus and extending upward and is called the *pyramidal lobe.* The thyroid is enveloped by a *capsule* of connective tissue, from the deep surface of which a number of processes penetrate into the organ, dividing it into lobes and lobules. Each *lobule* is made up of numerous closed vesicles filled with a viscid, semifluid, colloid material. Vessels and lymphatics are very numerous throughout the gland.

Arterial supply: Superior and inferior thyroid.

Veins: Superior, middle, and inferior thyroid.

Nerve supply: From the middle and inferior cervical ganglia of the sympathetic system.

Describe the origin and development of the thyroid gland.

The thyroid gland is of entodermal origin. At about that time the demarcation of the primitive foregut begins, an outgrowth or diverticulum makes its appearance from the ventral wall of the cranial portion of the foregut. It is the rudiment of the thyroid gland. As growth proceeds this diverticulum, or *"bud,"* expands, while its stalk narrows down and forms the *thyroglossal duct.* The latter becomes obliterated, but a vestige remains in the adult in the form of the *foramen caecum* of the tongue. Around the pharyngeal opening of the duct an elevation—the *tuberculum impar*—appears that either disappears entirely or forms part of the tongue and the *isthmus* of the thyroid gland. Later the "bud" becomes bilobed and has a divided lumen, which disappears in turn, and differentiation into isthmus and two lateral lobes is established. At the same time there is a steady movement downward (caudalward). The formation of *vesicles* in the gland begins about the tenth week and is not completed until after birth.

The *pyramidal lobe,* which is sometimes double and is present in about 40 per cent of individuals, extends upward toward the hyoid bone in front of the cricoid and thyroid cartilages. It is due to the development of gland tissue from the double lumen of the "bud," which becomes partly fused. Sometimes the rudiment develops into the *ligamentum suspensorium* or *m. levator glandulae thyreoideae.*

Describe the coccygeal (Luschka's) glomus (body).

The *coccygeal glomus* is a small body about the size of a pea, lying near the coccyx in a tendinous interval formed by the union of the levator ani muscles. It consists of small freely communicating blood vessels surrounded by several layers of polyhedral granular cells. The whole structure is invested in a capsule of connective tissue. Nerves derived from the sympathetic system pass to it.

Describe the thymus.

The thymus is a lymphoid organ weighing about 15 gm. at birth (5 cm. by 4 cm. and about 6 cm. in thickness) and attaining its greatest relative development about the second year, but continuing to grow until puberty. After that it diminishes in size, but does not disappear entirely, the lymphoid tissue being converted into fat. In the newborn child it has a pinkish color and is composed of *two lateral lobes* separated by a *fissure.* The main portion is placed in the superior and anterior mediastinum; as a rule, it extends downward as far as the fourth costal cartilage.

Structure: The thymus is composed of a large number of small polyhedral lobules; each lobule is composed of a cluster of lymphoid follicles with a small amount of delicate connective tissue intervening between them. Contained in the follicles are the concentric *corpus-*

cles of Hassall. These corpuscles are composed of flattened cells arranged concentrically around a granular nucleated cell. The gland is surrounded by a fibrous sheath, which sends prolongations between the different lobules.

What are the suprarenal glands and what are their relations to adjacent organs and parts?

They are two triangular organs that lie one on either side of the vertebral column in intimate relation with the upper end of the corresponding kidney. In structure they consist of a fibrous network supporting glandular tissue; the gland substance is composed of an external *cortical layer,* which is firm in consistency and yellow and forms the chief bulk of the organ; and an internal *medullary layer of chromophile tissue,* very soft and pulpy in consistency and dark in color. The *left suprarenal* rests on the superior and inner surface of the left kidney; the anterior surface is in relation with the posterior surface of the stomach and pancreas; the posterior surface is in relation with the left crus of the diaphragm and left kidney. The *right suprarenal* rests by its base upon the anterior and inner aspect of the right kidney; it is situated between the posterior surface of the right lobe of the liver and that portion of the diaphragm which covers the side of the vertebrae; the vena cava rests on the inner surface.

NERVOUS SYSTEM

The Brain

Give the subdivisions of the central nervous system and the important structures contained in each.

(1) *Spinal medulla* or spinal cord.

(2) *Hindbrain* or rhombencephalon (so called from the rhomboid shape of the fourth ventricle as seen from above), comprising the medulla oblongata, pons varolii, and cerebellum; the isthmus; and the fourth ventricle, a continuation of the central canal of the spinal cord.

(3) *Midbrain* or mesencephalon, comprising the pedunculi cerebri; corpora quadrigemina; the brachia conjunctiva (superior cerebellar peduncles); aqueductus cerebri (aqueduct of Sylvius) connecting the fourth and third ventricles; tegmentum and red tegmental nucleus.

(4) *Forebrain* or prosencephalon made up of the two cerebral hemispheres; the cortex or pallium above, the optic thalamus (anterior tubercle and pulvinar, internal capsule); the corpus callosum at the bottom, connecting the two hemispheres; pineal body; hypophysis cerebri with infundibulum and tuber cinereum; third ventricle; lateral ventricles in the interior of the cerebral hemisphere; optic tract and optic chiasm.

The space between and below the cerebral hemispheres is called the *interbrain* or diencephalon.

Describe the dura mater. Mention the processes and sinuses of the dura mater.

The *dura mater* is a dense fibrous membrane consisting in some areas of two layers and lined on the inner surface by endothelium. It is divided into cranial and spinal portions. The *cranial dura* is adherent to the inner surface of the cranial wall and performs a double office: it forms the inner periosteum of the skull and also envelops and protects the brain. It is intimately adherent at the line of the sutures and around the foramen magnum, and at the base of the brain and exit of nerves. At definite places it contains the *cranial sinuses.* The *spinal dura,* elastic in character, invests the cord from the foramen magnum to the third sacral vertebra and supplies a sheath to the spinal nerves where they emerge from the cord. It is separated from the vertebrae by fat and vessels.

The *processes* are: the falx cerebri, tentorium cerebelli, falx cerebelli, and the diaphragma sellae. The *cranial sinuses* are: the superior and inferior sagittal, straight, anterior and posterior intercavernous (circular), and basilar (unpaired); and the transverse (lateral), occipital, cavernous, superior and inferior petrosal, and sphenoparietal (paired).

Describe the arachnoid.

✓ It is a delicate membrane, lying between the pia and the dura, which bridges over the convolutions. It consists of interwoven bundles of fibrous and yellow elastic tissue covered with a layer of *endothelium*. The pacchionian bodies develop from this layer. The cerebrospinal fluid cisterns lie between it and the pia.

Describe the pia mater.

✓ The *pia* is the innermost of the three meninges and forms the immediate investment of the brain and cord. It supports the blood vessels, dips down into the sulci, and passes into the ventricular cavity. The membrane is thicker and denser in the cord.

Describe the hemispheres and lobes of the brain.

The cerebral hemispheres are ovoid, convex on their superior and lateral surfaces, partially separated from each other by the longitudinal fissure, but connected by the corpus callosum.

Each *hemisphere* has five lobes and eight fissures. The *frontal lobe* is bounded internally by the longitudinal fissure, below by the lateral (sylvian), and posteriorly by the central (rolandic) fissures. The *parietal lobe* extends from the longitudinal fissure downward to the lateral fissure and anteroposteriorly from the central fissure to the parieto-occipital fissure; the *occipital lobe* lies behind the parieto-occipital fissure; the *temporosphenoidal* occupies the middle fossa of the skull and is bounded in front by the lateral fissure; the *central lobe, insula,* or island of Reil lies in the lateral fissure, covered by the frontal and temporosphenoidal lobes.

Give a method by which the lateral and central fissures may be approximately mapped out on the surface of the skull.

Lateral Fissure: Draw a line from a point 1¼ inches horizontally behind the external angular process of the frontal bone to a point ¾ inch below the parietal eminence.

Central Fissure: From a point ½ inch behind the midpoint of a line connecting the glabella and the external occipital protuberance draw a line, 3¾ inches in length, over the side of the head at an angle of 67 degrees with the median line

Where is the lateral fissure and what artery does it contain?

The fissure separates the frontal and parietal lobes from the temporal; it begins at the anterior perforated space and passes outward and upward to the external surface of the hemisphere. It contains the middle cerebral artery.

In the anatomy of the brain what is the corpus callosum? Describe its connections.

It is a thick, arched layer of transverse fibers at the bottom of the longitudinal fissure; *anteriorly,* it curves upon itself and gives off two peduncles at the entrance of the lateral fissure; *posteriorly,* it is continuous with the fornix. It forms the roof of the lateral ventricles. A median depression on its upper surface is called the *raphe,* parallel to which, on each side, run two or more elevated bands, the *striae longitudinales.*

Mention the more important connecting tracts in the brain.

(1) *Pedunculi cerebri*—from the pons to the cerebral hemispheres.

(2) *Restiform bodies* or inferior peduncles of cerebellum—from the medulla oblongata to the cerebellum.

(3) *Brachium pontis* or middle pe-

duncle of pons—from pons to cerebellum.

(4) *Brachia conjunctiva* (superior cerebellar peduncles)—from cerebellum to cerebrum along the dorsal surface of the pons.

(5) *Corpus callosum* at the bottom of longitudinal fissure—connecting the two cerebral hemispheres.

Give a brief general description of the appearance of the brain when viewed from below.

The base of the brain—*basis cerebri*—exhibits, from below upward, the following structures:

The cylindrical *medulla oblongata* with the prominent *pyramids* and *olives*, occupying the hollow or *vallecula* between the two *cerebellar hemispheres*. Above the medulla oblongata and cerebellum, the *pons varolii*, the great "bridge" between the rhombencephalon and the meso- and prosencephalon, with the *pedunculi cerebri* connecting the pons with the cerebral hemispheres. The under surfaces of the temporal and orbital portions of the frontal lobes and the *transverse cerebral fissure* separating the cerebellum from the cerebrum. In the space between the upper border of the pons below and the optic chiasm above, the prominent *hypophysis cerebri* (pituitary body) with its stalk or *infundibulum* and *tuber cinereum*. Next, the *optic tracts, optic chiasm,* and *optic nerves* and, above, the *olfactory tracts* and *bulbs* lying on the under surface of the frontal lobes with the deep longitudinal fissure between, dividing the two *cerebral hemispheres*.

What are the basal ganglia of the brain? Mention some of the more important ones.

They are masses of gray matter embedded in the white substance chiefly of the midbrain. The most important are:

(*a*) The *caudate* and *lentiform nuclei* above the thalamus, together forming the *corpus striatum,* an important structure that exercises a controlling and coordinating influence on voluntary muscles used for delicate movements requiring accurate coordination. Lesions of the corpus striatum affect articulation, swallowing, and other similar movements.

(*b*) The *thalamic nuclei:* lateral, anterior, and posterior thalamic nuclei; (*c*) *pulvinar;* (*d*) medial and lateral *geniculate bodies;* (*e*) *red nucleus* in the hypothalamic region; (*f*) amygdaloid *nucleus.*

The *internal capsule* is a band of white matter lying between the caudate and the lentiform nucleus. It is divided into an anterior and a posterior limb. The latter contains the great motor or cerebrospinal tract conveying fibers from the cerebral cortex to the nuclei of cranial nerves and to motor cells in the anterior column of gray matter in the spinal medulla.

Name and bound the ventricles of the brain.

Two lateral, third, fourth, and fifth. The boundaries are:

Lateral: Roof, corpus callosum; floor, caudate nucleus, corpus striatum, taenia thalami, optic thalamus, choroid plexus, fimbria, and fornix; medially, the septum pellucidum; laterally, the brain substance.

Third: Roof, tela chorioidea (velum interpositum), lateral walls by optic thalami and peduncles of pineal body; floor, tuber cinereum, corpora mammillaria, and the posterior perforate space; in front, the arteria crura of the fornix and part of the anterior commissure; behind, the posterior commissure.

Fourth: Roof: the cerebellum and the anterior medullary velum; the floor, the posterior surface of the medulla and pons; laterally, bounded by the superior, middle, and inferior peduncles of the cerebellum.

Fifth Ventricle: The space between the two layers of the septum lucidum; it is covered by the corpus callosum. This does not normally connect with the system.

Trace the cerebrospinal fluid from the lateral ventricles to the spinal canal.

From the lateral ventricles, through the interventricular foramen (foramen of Monro), into the third ventricle; thence through the aqueduct (of Sylvius) into the fourth ventricle, through the latter, and to the microscopic central canal of the spinal cord. From the fourth ventricle through the median and lateral apertures to the subarachnoid spaces.

Give the location and the description of corpora quadrigemina.

They consist of four rounded eminences on the posterior aspect of the midbrain. The *superior* pair are larger and broader than the *inferior,* and are connected to the brain by tracts of white fibers called *brachia.* The superior pair give origin to the optic tracts, the inferior to the cochlear division of the eighth nerve. The quadrigemina consist of white matter medially and gray laterally.

Locate the fourth ventricle of the brain.

It is the space between the posterior surface of the medulla and pons in front and the cerebellum behind. Lateral boundaries: superior cerebellar peduncle or *brachium conjunctivum;* middle, or *brachium pontis;* and inferior, or *restiform body.*

Medulla and Spinal Cord

Describe the medulla oblongata.

It is the upper, enlarged portion of the spinal cord, extending from the upper border of the atlas or decussation of the pyramidal tracts to the lower border of the pons. The *posterior surface* forms the lower half of the fourth ventricle; its *anterior surface* rests on the basilar groove of the occipital bone. The medulla is divided into two lateral halves by the anterior and posterior median fissures. From the sides of the medulla the ninth, tenth, cranial portion of the eleventh, and twelfth nerves arise. It contains vasomotor, cardiac respiratory, deglutition, and mastication centers.

The anterior pyramid is formed by the lateral and anterior cerebrospinal fasciculi (crossed and direct pyramidal tracts). The fibers of the former decussate at the lower part. Projecting from the upper part is an oval bulge, the olive, overlying a capsule of gray matter, the inferior olivary nucleus. The outer portion of the olive is in relation with the lateral fasciculus, which lies in front of the restiform body. The latter is the continuation of the fasciculus spinocerebellaris and passes above into the corresponding hemisphere of the cerebellum, forming the inferior peduncle. On either side of the posterior fissure lies the fasciculus gracilis. The fasciculus cuneatus and the fasciculus gracilis represent the continuation of the columns of Burdach and Goll respectively.

Give a brief general description of the spinal medulla or spinal cord.

The spinal medulla is that part of the cerebrospinal axis which occupies the upper two thirds of the vertebral canal. It is a cylindrical structure, slightly flattened from before backward, and partially divided by two *fissures,* a shallow anterior, and a deep posterior. It extends from the foramen magnum above to the level of the first lumbar vertebra and has a length of about 45 cm. The medulla is lodged in the vertebral canal, suspended by winglike lateral attachments, the *ligamenta denticulata.* From the spinal medulla issue the 31 pairs of spinal nerves: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal. The cord is continuous above with the medulla oblongata and ends in the *cauda equina,* a sheaf of nerve roots from the sacral and lumbar regions having in its center the *filum terminale.* The cord presents two conspicuous *enlargements,* one in the cervical and one in the lumbar region, corresponding to the spinal segments which give rise to the nerves that control the muscles of the upper and lower extremity respectively.

Describe the structure of the spinal medulla and the general arrangement of the gray and white matter.

The spinal medulla is made up of *gray matter* and *white matter,* the former consisting mainly of nerve cells and their axons and dendrites, the white matter of medullated fibers, the whole held together by an interlacing network of *neuroglia.* The gray matter occupies the central portion and is surrounded by the white matter, which forms the greater part of the cord. In cross section the gray matter appears in the shape of a letter H, presenting *two anterior* and *two posterior columns* (horns), joined by two commissures, an anterior white and a posterior gray commissure. The anterior column is *motor,* the posterior *sensory.* In the center of the gray commissure is the *central canal,* which is continuous above with the fourth ventricle of the brain.

Gray Matter: This consists chiefly of nerve cells with a main central fiber or *axon,* which becomes the *axis-cylinder* of a nerve fiber, and a number of *dendrites* held together by neuroglia. These nerve cells are arranged in three columns:

(1) *Ventral cell column* in the anterior horn is composed chiefly of motor nerve cells.

(2) *Intermediolateral column,* the cells of which give off very fine fibers that, for the most part, form the *white rami communicantes* of the sympathetic ganglia.

(3) *Nucleus dorsalis* (Clarke's column)—so called because it is confined to the dorsal (thoracic) region—the axons of which form the *fasciculus spinocerebellaris* (direct cerebellar tract) of the white matter.

The nerve fibers of the gray matter are of three kinds (*a*) collateral or connecting; (*b*) terminations of nerve fibers; (*c*) axons given off by nerve cells.

White Matter: This consists of medullated fibers arranged in *funiculi* or tracts, the funiculi being further subdivided into *fasciculi* or bundles.

(1) *Posterior funiculus,* made up of the *fasciculus cuneatus* (column of Burdach) and the *fasciculus gracilis* (column of Goll), contains sensory fibers that enter the spinal medulla by the posterior roots.

Association fibers.—the posterior funiculus also contains fibers that do not enter by the posterior roots but divide into ascending and descending branches, forming connections between the different parts of the spinal medulla, and constituting the *fasciculus posterior proprius.*

(2) *Fasciculus posterolateralis* (tract of Lissauer) is composed of very small fibers that enter the posterior roots and end in the substantia gelatinosa.

(3) *Anterolateral funiculus* comprises all that part of the white matter not contained in the posterior funiculus. It is made up of the following fasciculi:

(*a*) *Fasciculus anterior proprius* and (*b*) *fasciculus lateralis* is composed of *intrinsic* fibers, *i.e.,* fibers from the nerve cells in the gray columns that end in the gray matter.

(*c*) *Fasciculus cerebrospinalis lateralis* (crossed pyramidal tract). (*d*) *Fasciculus cerebrospinalis anterior* (direct pyramidal tract). (*e*) *Fasciculus spinocerebellaris* (direct cerebellar tract). (*f*) *Fasciculus anterolateralis superficialis* (Gower's tract).

The last four are *extrinsic,* or long system, fibers. The fasciculus cerebrospinalis lateralis is a decussating, or crossed, *descending* tract and is the great *motor tract* that brings the spinal motor apparatus under the control of the will. The cerebrospinalis anterior is also a descending tract deriving from the motor area of the cortex of the same side as the former. Its fibers, however, cross in the anterior (white) commissure to end in ventral (anterior) motor cells in the other side of the cord. The fibers of both these tracts therefore pass from the cortex of one side to motor cells in the opposite side of the spinal medulla.

The spinocerebellar and superficial anterolateral fasciculi are *ascending* tracts that convey sensory fibers from muscles and overlying skin to the cerebellum, and are essential to the function of coordination of muscular movements.

✓

The Cranial Nerves

Name the twelve pairs of cranial nerves.

I, Olfactory; II, optic; III, oculomotor; IV, trochlear; V, trigeminal, VI, abducens; VII, facial; VIII, stato-acoustic; IX, glossopharyngeal; X, vagus; XI, accessory (spinal accessory); and XII, hypoglossal.

Give the origin and distribution of the olfactory nerve.

Sensory. Not a single bundle. About twenty small nerves arise from the under surface of the olfactory bulb of either side. They pass through the foramina in the cribriform plate of the ethmoid bone to enter the nose and are distributed as nerves of smell to the mucous membrane of the upper third of the nasal septum, the roof of the nose, and the upper third of the lateral wall.

Describe the course of the nerve fibers in the optic commissure.

The fibers upon the posterior surface of the optic chiasm (Gudden's commissure) have nothing to do with sight; they unite the superior quadrigeminal bodies. The middle fibers decussate, those from the right optic tract passing to the left optic nerve and vice versa, to terminate in the nasal half of the retina. The outermost fibers of each tract do not decussate, but pass into the optic nerve of the same side and are distributed to the temporal half of the retina of the same side.

Describe the origin and distribution of the optic nerve.

Sensory. The nerve arises from the optic commissure, pierces the dura, and passes from the cranial cavity into the orbit, through the optic foramen. In the orbit it is attached to the posterior pole of the eyeball at a point $\frac{1}{8}$ inch on the medial side of the longitudinal axis. The nerve fibers pierce the fibrous and vascular coats to form the innermost layer of the retina.

Give the function and distribution of the oculomotor cranial nerve.

Motor. It is the *motor* nerve to all the extra-ocular muscles except the lateral rectus and superior oblique; it also supplies the iris and ciliary muscle and the short or motor root of the ciliary ganglion.

State the origin, function, and distribution of the trochlear cranial nerve.

Motor. *Deep origin* from the floor of the aqueduct; *superficial origin* from behind the corpora quadrigemina. It is the *motor* nerve to the superior oblique muscle.

Give the origin and functions of the trigeminal (fifth cranial) nerve and name the divisions of the same.

Mixed. It arises from the side of the pons by two roots, a *motor* and a *sensory*. *Functions:* sensory nerve of the head and face, and motor nerve of the muscles of mastication. *Divisions:* ophthalmic, maxillary (superior maxillary), mandibular (inferior maxillary). The first two divisions are sensory, third is both sensory and motor.

Name the ganglia connected with the fifth pair of cranial nerves.

The sensory ganglion is the semilunar (trigeminal or gasserian); the autonomic ganglia are the ciliary, sphenopalatine (Meckel's), otic, and submaxillary.

State the origin of the sensory division of the fifth pair of cranial nerves.

Deep origin is from a nucleus in the pons just below the floor of the fourth ventricle; *superficial origin,* from the side of the pons.

Give the origin and distribution of the third division of the fifth pair of nerves.

The *sensory root* originates from the semilunar ganglion; the *motor root,* from the side of the pons varolii. The roots unite and pass out of the skull through the foramen ovale, immediately dividing into anterior and posterior trunks.

The *anterior trunk,* principally motor, gives off branches to the meninges and to the muscles of mastication; the *posterior trunk,* largely sensory, divides into the inferior alveolar, auriculotemporal, and lingual. The inferior alveolar gives a motor branch to the mylohyoid muscle and sensory branches to the teeth of the lower jaw; the auriculotemporal supplies the external meatus, parotid gland, temporomaxillary articulation, and temple; the lingual nerve is joined by the chorda tympani branch of the facial nerve beneath the external pterygoid muscle and supplies the anterior two thirds of the tongue.

State origin, course, function, and distribution of abducens nerve.

Motor. *Superficial origin* is from groove between the anterior pyramid of the medulla and the pons; *deep origin* from the floor of the fourth ventricle. The nerve pierces the dura in the posterior fossa of the base of the skull to enter the cavernous sinus, where it lies to the outer side of the internal carotid artery. It enters the orbit through the superior orbital fissure, passes between the two heads of the lateral rectus muscle, and terminates in its fibers. *Function:* motor nerve to the lateral rectus muscle.

Give origin, course, and distribution of the facial nerve.

Mixed. *Deep origin* is from a nucleus in the pons; *superficial origin* from the lateral border of the groove between the medulla and the pons. The nerve pierces the dura and enters the internal acoustic meatus with the eighth nerve, and, at the bottom of the meatus, it passes into the canalis facialis (Fallopian aqueduct or canal). In this canal it traverses the petrous portion of the temporal bone, making its exit from the skull through the stylomastoid foramen; it passes first lateral then forward in the substance of the parotid gland and divides into numerous branches at the anterior border to supply the buccinator muscle and the muscles of expression. This nerve sends communications to the fifth, eighth, ninth, tenth, and sympathetic nerves.

Where does the glossopharyngeal nerve rise, and what structures are supplied by this nerve and its branches?

Mixed. *Deep origin* is from the floor of the fourth ventricle; *superficial origin,* from the upper portion of the medulla in the groove between the olive and the restiform body. The ninth nerve is the nerve of *sensation* to the mucous membrane of the pharynx, fauces, tonsil, and posterior third of the tongue; it also supplies the stylopharyngeus muscle and sends a branch to the tympanum (Jacobson's nerve). It is the nerve of *taste* for the posterior third of the tongue.

What nerves form the pharyngeal plexus?

Pharyngeal branches of the glossopharyngeal, vagus, and cervical sympathetic.

What cranial nerve has the widest distribution?

Mixed. Vagus (tenth).

Give the five principal points of distribution of the vagus nerve.

Muscles of pharynx and sympathetic ganglia of thorax and abdomen and by these to the heart, smooth muscle and glands, posterior taste buds, skin of the ear canal; sensory to the pharynx and larynx; and afferent to the heart, lungs and digestive tract.

Give the deep and superficial origin, course, and distribution of the vagus nerve.

Deep origin is from a nucleus in the lower part of the floor of the fourth ventricle; *superficial origin* from the groove between the olive and restiform body, below the glossopharyngeal nerve. It *supplies* the organs of voice and respiration with *motor* and *sensory fibers;* and the pharynx, esophagus, stomach, and heart with *motor* fibers.

Give the origin and distribution of the eleventh or accessory (spinal accessory) cranial nerve.

Motor. It has two origins: one, from the side of the medulla; the other, from the spinal cord as low down as the sixth cervical nerve. The nerve supplies the sternomastoid and trapezius muscles.

Give the origin and distribution of the hypoglossal nerve.

Motor. *Deep origin* is from the floor of the fourth ventricle; *superficial origin,* from the groove between the pyramid and olive of the medulla. The nerve receives fibers from the first and second cervical nerves, which leave the nerve as the descending branch of the hypoglossal and thyrohyoid branches. The twelfth nerve is the *motor* nerve of the tongue.

What nerves supply the tongue?

Motor, hypoglossal; *sensory,* the gustatory branch of the fifth and superior laryngeal branch of the tenth; *taste,* glossopharyngeal, and chorda tympani through anastomosis with gustatory branch of fifth.

What are the nerves of the eyeball?

Optic, motor oculi, and ophthalmic division of fifth (both through ciliary ganglion), and sympathetic fibers from cavernous plexus (also to ganglion).

The Spinal Nerves

Describe the phrenic nerve.

Derived from the third, fourth, and fifth cervical nerves, it passes downward in the neck, upon the scalenus anterior muscle, and traverses the superior and anterior mediastinum to reach the diaphragm, lying between the pleura and pericardium in front of the root of the lung. *Branches* are muscular (to the diaphragm); pleural, pericardial, inferior vena caval, suprarenal, and hepatic.

What constitutes the brachial plexus?

The plexus is formed by the anterior rami of the *fifth, sixth, seventh,* and *eighth cervical,* and the *first thoracic* nerves, with a small slip from the fourth cervical. The nerves unite and form *three primary cords;* these cords divide and form *three secondary cords,* from which the terminal nerves are given off. *Branches* arise from the cords and nerves.

Describe the radial nerve.

The nerve is one of the terminal branches of the posterior cord of the brachial plexus. The nerve passes from the medial to the lateral side of the arm, through the groove for the radial nerve (musculospiral groove) and in front of the lateral condyle; the nerve divides into the *superficial* (radial nerve) and *deep* (posterior interosseous nerve) *rami.* The remaining *branches* are muscular, nutrient, and cutaneous. It supplies all of the muscles making up the mass about the radial epicondyle.

Give the distribution of the superficial ramus of the radial nerve below the wrist.

The nerve is entirely cutaneous. It supplies the radial half of the dorsum of the wrist and hand, dorsum of thumb, index, and radial half of middle fingers excepting distal phalanx. Its branches communicate with the musculocutaneous nerve and dorsal branch of the ulnar.

Give the origin and distribution of the median nerve.

The nerve is formed by the union of a branch from the medial and one from the lateral cord of the brachial plexus and passes down the arm in close relation with the brachial artery. At the bend of the elbow it passes between the two heads of the pronator radii teres to run between the deep and superficial flexors to within 2 inches of the wrist, where it becomes superficial.

The nerve gives off no branches in the arm. In the forearm it supplies the flexors and pronators of the wrist, excepting the flexor carpi ulnaris and the radial one half of the flexor profundus digitorum; it also supplies the abductor, opponens, and radial head of the flexor brevis pollicis with the two outer lumbricales. It is the *cutaneous nerve of the radial side* of the palm and palmar surface of the thumb, index, middle, and one half of the ring fingers, also of the dorsum of the last phalanx of the fingers.

Describe the course and distribution of the nerves of the palm of the hand.

The *median nerve* enters the palm of the hand on the lateral (radial) side of the flexor tendons of the fingers, beneath the transverse carpal (annular) ligament, first giving off a palmar cutaneous, which supplies the palmar cutaneous surface of the thumb, index, middle, and one half of the ring fingers. The *main muscular branch* supplies the abductor, opponens, and outer head of the flexor brevis pollicis. Fine muscular branches to the two outer lumbrical muscles arise from digital branches to the contiguous sides of the index and middle, and middle and ring fingers respectively.

The *ulnar nerve* gives off palmar cutaneous branches to the little and ring fingers, and sends a deep palmar branch between the abductor and flexor brevis minimi digiti, which follows the deep palmar arch across the palm. In its course it supplies branches to the following muscles: interossei, third and fourth lumbricales, oblique and transverse adductores pollicis, and the deep part of the flexor pollicis brevis. Articular branches to the wrist are also derived from this nerve.

Describe the sacral plexus and name its branches.

It is the sacral portion of the lumbosacral plexus and is formed by the fourth and fifth lumbar, and the first two or three sacral nerves. It is placed on the posterior wall of the pelvis between the parietal pelvic fascia and the piriformis muscle. In front are the pelvic colon, hypogastric vessels, and the piriformis muscle. It supplies the lower extremity.

The nerves forming the plexus unite to form the *sciatic nerve*, which ends in the thigh by dividing into the *tibial* and *common peroneal* nerves.

Branches: Anterior or *ventral*—tibial gives nerves to hamstring muscles, quadratus femoris, gemelli, obturator internus; articular branches to hip joint. *Posterior* or *dorsal*—common peroneal gives nerves to short head of biceps, and piriformis muscles; superior and inferior gluteal; articular branches to knee joint.

Give the origin, course, and distribution of the sciatic nerve.

Origin is from the lumbosacral cord and first, second, and third sacral nerves. After arising from the above nerves it passes out of the pelvis through the *great sacrosciatic foramen* below the piriformis muscle, descends between the great trochanter and the tuberosity of the ischium, and passes down the back of the thigh to its lower third, where it divides into the tibial and common peroneal. The nerve sends branches to the hip and knee joints and supplies the hamstring muscles of the thigh and all muscles below the knee, and the skin of the leg and foot.

The Sympathetic Nervous System

Describe the sympathetic nervous system, its principal ganglia and plexuses.

The sympathetic nervous system consists of a pair of *gangliated trunks*, situated on each side of the vertebral column and connected to the peripheral spinal nerves by one series of nerves and to the viscera by another series. Each trunk enters the cranial cavity with the internal carotid artery, on which it forms plexuses; at the distal or caudal end the two trunks are joined together and terminate in the *coccygeal ganglion* or *ganglion impar.*

The *efferent* branches, which pass from the spinal nerves to the viscera and vessels, are formed of medullated fibers —the *white rami communicantes* (visceral branches of the spinal nerves). The *gray rami communicantes,* consisting of nonmedullated fibers, are derived from the axons of the sympathetic *ganglion cells* and pass *centrally* from the ganglia to the spinal nerves. Some also help to form the *commissural cord* which connects the ganglia.

The *peripheral* branches of the sympathetic nervous system consist of (1) *white fibers,* which may be splanchnic afferent or splanchnic efferent; and (2) *gray fibers,* which are efferent and distributed to unstriped muscular fibers (vasomotor, pilomotor) and glands (secretory).

Ganglia: The gangliated trunks are customarily divided into four parts: cervical, thoracic, abdominal, and pelvic.

The *cervical ganglia* are three in number: a *superior,* situated at the base of the skull between the internal jugular vein and the internal carotid artery; a *middle,* placed over the inferior thyroid artery behind the carotid sheath (it is frequently absent); the *inferior* cervical ganglion, behind the subclavian artery opposite the transverse process of the seventh cervical vertebra.

The number of ganglia in the remaining three portions is variable, some of the units being fused together. There are usually 10 or 11 thoracic; 4 (up to 8) abdominal; and 4 pelvic. At the pelvic end the two trunks are united in the coccygeal ganglion or ganglion impar. All the ganglia are connected by the commissural cord.

Plexuses: The peripheral branches of the sympathetic form or join plexuses in their neighborhood.

The cervical ganglia form the *carotid* and *cavernous plexuses;* the external carotid, pharyngeal, thyroid, vertebral and subclavian plexuses; and send branches to the *cardiac plexuses.*

The thoracic ganglia send branches to the *pulmonary* and *esophageal plexuses.* They also form plexuses on the thoracic aorta and contribute to the formation of the celiac plexus by means of the splanchnic nerves.

The *celiac, hypogastric,* and *pelvic plexuses* are formed by peripheral branches of the lower thoracic, abdominal, and upper pelvic parts of the sympathetic trunks. They distribute nerves to the viscera and vessels of the abdominal and pelvic cavities.

Describe the celiac (solar) plexus.

The plexus consists of a network of nerves—the *celiac plexus*—surrounding the origin of the celiac artery and of the *two celiac ganglia,* situated on the crura of the diaphragm. The greater splanchnic nerve from above and the lesser splanchnic nerve from below take part in the formation of the plexus. The plexus lies on the posterior abdominal wall between the crura of the diaphragm and behind the stomach.

Give a brief description of the splanchnic nerves.

There are three: greater, smaller, and lowermost.

The *greater splanchnic nerve* arises from the fifth to the ninth thoracic ganglia of the sympathetic, pierces the crus of the diaphragm, and joins the anterior (upper) end of the celiac plexus. The *splanchnic ganglion* is formed upon the thoracic portion of the nerve.

The *smaller splanchnic nerve* arises from the ninth and tenth thoracic ganglia, pierces the diaphragm along with the greater, and ends in the *aorticorenal ganglion* at the posterior (lower) end of the celiac plexus.

The *lowermost splanchnic nerve* arises from the last thoracic ganglion or may be a branch of the smaller splanchnic. It ends in the *renal plexus.*

THE MUSCLES

Give boundaries of the anterior triangles of the neck and give the origin and insertion of the muscles forming the boundaries.

The *anterior triangle* is bounded above by the lower jaw, anteriorly by the middle line of the neck, and posteriorly by the anterior border of the sternomastoid muscle. This triangle is subdivided into three smaller triangles by the anterior belly of the omohyoid and the digastric.

The inferior carotid or *muscular triangle* is bounded anteriorly by the midline of the neck, behind by the sternomastoid, above by the anterior belly of the omohyoid. The *superior carotid triangle* is bounded below by the anterior belly of the omohyoid, behind by the sternomastoid, above by the posterior belly of the digastric. The *submaxillary triangle* is bounded below by the digastric, above by the lower jaw.

Sternocleidomastoid: Origin, upper part of the sternum and inner portion of the clavicle; insertion, mastoid process and superior curved line of the occipital bone.

Omohyoid: Origin, upper border of the scapula near the suprascapular notch; insertion into the body of the hyoid bone. This muscle has two bellies connected by a central tendon, which is attached to the first rib by a band of deep fascia joining the muscle at the angle between the bellies.

Give the origin, insertion, action, and nerve supply of any of the following muscles: superior oblique, masseter, and trapezius.

The *masseter* muscle has two origins, a *superficial* portion from the anterior two thirds of the lower border of the zygomatic arch, and a *deep* portion from the deep surface of the zygomatic arch posteriorly. The muscle is inserted into the lateral surface of the ramus and angle of mandible and coronoid process. *Action:* to close the mouth; protrusion, retraction, and lateral movements of jaw (chewing). *Nerve supply:* motor branch of the fifth, accompanying the mandibular division.

Name the seven muscles of the orbit.

Levator palpebrae superioris; inferior, superior, lateral, and medial recti; superior and inferior oblique.

Give the names of the principal muscles of the back.

Trapezius, latissimus dorsi, rhomboideus major and minor, sacrospinalis (erector spinae), and multifidus spinae.

Locate and describe the quadratus lumborum muscle and give its important relations.

The muscle is situated in the lumbar region and is regularly quadrilateral in shape. It arises by aponeurotic fibers from the iliolumbar ligament, the crest of the ilium, and the lower lumbar vertebrae; it is inserted into the lower border of the last rib for about half its length, and, by four small tendons, into the transverse processes of the four upper lumbar vertebrae. The anterior surface of the muscle is in relation with the colon and kidneys.

Name five muscles of the shoulder and give the origin and insertion of any one.

Pectoralis major and minor, deltoid, subscapularis, supra- and infraspinatus.

Pectoralis minor: Origin from the third, fourth, and fifth ribs near the cartilages; insertion into the coracoid process.

Give the origin, insertion, and action of any one of the following muscles: occipitofrontalis, deltoid, and gastrocnemius.

The *deltoid* arises from the lateral third of the anterior border of the clavicle, the lateral margin of the acromion, and entire length of the lower border of the spine of the scapula. It is inserted into the deltoid impression upon the anterior lateral surface of the middle of the shaft of the humerus. Its action is to abduct the arm to a horizontal position, and inward and outward rotation.

Give the origin and insertion and blood and nerve supply of the biceps brachii muscle.

The origin of the short head is from the coracoid process of scapula; long head, from the upper margin of the glenoid cavity. The muscle is *inserted* into the tuberosity of the radius and by a membranous band (the *lacertus fibrosus*) into the fascia of the forearm. *Blood supply* is from the brachial artery. *Nerve supply* is from the musculocutaneous.

Name and give the origin of the muscles inserted into the greater and lesser tuberosities and edges of the intertubercular (bicipital) groove of the humerus.

Inserted into the large tubercle (greater tuberosity) are the following muscles: supra- and infraspinatus, and teres minor; into the lesser, the subscapularis; into the intertubercular groove, the pectoralis major, teres major, and latissimus dorsi.

The *supraspinatus* arises from the medial two thirds of the fossa of the same name; the infraspinatus, from the medial two thirds of the infraspinous fossa. The *teres minor* arises from the upper two thirds of the dorsal surface of the axillary border of the scapula and intermuscular septum.

The *subscapularis* arises from the whole of the subscapular fossa and the groove along the axillary margin.

The *teres major* arises from the dorsal aspect of the angle of the scapula and intermuscular septum. The latissimus dorsi arises from the spinous processes of the lower six thoracic, all the lumbar and sacral vertebrae, the crest of the ilium, and the angles of the four lower ribs. The *pectoralis major* arises from the lower surface of the medial half of the clavicle, half the breadth of the sternum, cartilages of all of the true ribs, excepting the first and seventh, and from the aponeurosis of the obliquus abdominis externus.

Name five muscles of the shoulder and arm. Give the origin, insertion, and action of any one of the five.

Deltoid, biceps, triceps, teres major, and coracobrachialis.

The *coracobrachialis* arises from the coracoid process of the scapula and inserts into the middle of the medial border of the shaft of the humerus. *Action* is to assist the biceps in elevation and adduction of the arm.

Mention any one muscle that moves the humerus (a) forward, (b) backward, or (c) inward.

(*a*) Coracobrachialis; (*b*) posterior fibers of deltoid; (*c*) pectoralis major.

What are the anterior and posterior boundaries of the axilla, and what arteries and nerves pass through it?

The *anterior boundary* is formed by the pectoralis major and minor and the costocoracoid membrane; posterior boundary, the subscapularis and tendons of teres major and latissimus dorsi.

The *arteries* passing through the space are the axillary and its branches, as follows: supreme thoracic, thoracoacromial, lateral thoracic, anterior and posterior circumflex, and subscapular.

The *nerves* are the brachial plexus with the following branches: long thoracic, thoracodorsal (long subscapular), first or short subscapular, second or lower subscapular, medial and lateral anterior thoracic, axillary (circumflex), radial, musculocutaneous, median, medial cutaneous of forearm, and medial cutaneous of arm.

Mention the flexor muscles of the forearm and describe one of them.

Flexor carpi radialis, palmaris longus, flexor carpi ulnaris, flexor sublimis and profundus digitorum, flexor longus pollicis, pronator teres.

The *flexor carpi radialis* arises from the medial condyle by a common tendon with the other flexors from the deep fascia and intermuscular septum. It is inserted into the proximal ends of the second and third metacarpal bones. *Action* is flexion of the wrist, then of the forearm. *Nerve supply* is the median.

Describe the triangle of the elbow and name the structures that pass through it.

The cubital fossa or hollow of the elbow is bounded above by a line drawn between the two condyles of the humerus, laterally by the brachioradialis muscle, medially by the pronator teres muscle. The *floor* is formed by the brachialis anterior and supinator muscles. The *fossa* contains the brachial, radial, and ulnar arteries and veins, the median and radial nerves, and the tendon of the biceps.

Mention a muscle (a) which moves the thumb outward, (b) which moves the head forward, and (c) which moves the foot inward.

(*a*) Abductor pollicis; (*b*) longus capitis; (*c*) tibialis anterior.

Describe the palmar fascia.

The fascia consists of a central and two lateral portions; the central segment, triangular in form, is attached to the transverse carpal ligament and divides into four slips opposite the heads of the metacarpal bones; each slip again divides into two to enclose the flexor tendons. Strong transverse fibers connect the separate processes. The lateral portions of this fascia thinly invest the muscles of the thenar and hypothenar eminences.

Name three abdominal muscles and give the origin, insertion, and action of one of them.

External and internal oblique and rectus abdominis.

The *rectus* arises by an inner and outer head from the symphysis and crest of the pubis. It is inserted into the front of the xiphoid process and the fifth, sixth, and seventh costal cartilages.

What is the linea alba and how is it formed?

It is a tendinous raphe in the middle line of the abdomen, extending from the ensiform to the pubis. It is formed by the blending of the aponeuroses of the oblique and transversalis muscles.

State the action of each of the following muscles: masseter, tibialis anterior, and gluteus maximus.

The *masseter* raises the lower jaw against the upper and also protracts and retracts the jaw; the *tibialis anterior* extends (dorsiflexes) and inverts the tarsus upon the leg; the *gluteus maximus* is an extensor and a lateral rotator of the thigh.

What tissues of the abdominal wall are divided in the operation for appendicitis?

When the incision is made at McBurney's point, the following tissues are divided: skin, superficial fascia, external and internal oblique and transversalis muscles, transversalis fascia, preperitoneal fat, and peritoneum. When the incision is made in the right rectus, the following structures are divided: skin, superficial fascia, sheath of the rectus muscle, rectus muscle, transversalis fascia, preperitoneal fat, and peritoneum.

Describe the diaphragm, its principal openings, and nerve supply.

The *diaphragm* is a musculofibrous partition separating the cavities of the thorax and abdomen. The lower concave surface is in relation with the liver, stomach, spleen, kidneys and suprarenals, duodenum, and pancreas; the upper convex surface, rising higher on the right than on the left side, is in relation with the pericardium, pleura, and chest wall. It arises anteriorly from the xiphoid cartilage; laterally from the inner surface of the lower six ribs by fleshy bands that interdigitate with the transversalis muscle; posteriorly from the lumbar vertebrae by two crura.

The *opening* for the vena cava is situated in the right leaflet of the central tendon; the esophageal opening is in the muscular substance behind the central tendon; the aortic opening is situated between the crura and beneath the middle arcuate ligament.

The *nerve supply* is derived mostly from the phrenic, but also from the lower intercostals and sympathetic.

Mention the muscles attached to the greater trochanter of the femur.

Gluteus medius and minimus, piriformis, obturator internus and externus, and superior and inferior gemelli.

What forms the medial hamstrings?

The tendons of the semitendinosus, semimembranosus, and gracilis muscles.

Bound the femoral triangle and mention the vessels and nerve in it.

The triangle is bounded *above* by the inguinal ligament—*laterally* by the sartorius, *medially* by the adductor longus. The *floor* is formed by the iliacus, psoas, pectineus, adductor brevis, and longus muscles. The *vessels* in the triangle are the femoral arteries and veins. The anterior femoral *nerve* is contained in this triangle.

Describe the vessels, nerves and other structures found in the femoral (Scarpa's) trigone.

The *femoral artery* divides the triangle longitudinally into two nearly equal parts, extending from the middle of the base to the apex. It gives off the following branches: superficial epigastric, superficial circumflex iliac, and superficial and deep external pudendal arteries, and the profunda femoris.

The *femoral vein* lies to the medial side of the artery and receives the profunda tributaries which correspond with the branches of the femoral artery, and the *great saphenous vein.*

The *femoral nerve* lies lateral to the artery and divides into numerous branches. The trigone also contains fat and lymphatic nodes.

(a) Bound the abductor (Hunter's) canal. (b) What passes through it?

(*a*) The canal is bounded laterally by the vastus medialis, and medially by the adductor longus and adductor magnus; anteriorly these muscles are connected by fascia, upon which the sartorius muscle rests.

(*b*) The femoral vessels and their sheath and the saphenous nerve.

Bound the popliteal space. Mention its contents.

The space is bounded *above* by the external and internal hamstring muscles; *below,* laterally by the plantaris and outer head of the gastrocnemius muscles, medially by the inner head of the gastrocnemius. The *floor* is formed from above downward by the femur, posterior ligament of the knee joint, fascia covering the popliteus muscle, and the upper end of the tibia. The *roof* is formed by the fascia lata.

The space *contains* the popliteal vessels and branches and the termination of the small saphenous vein; the tibial and common peroneal nerves and the articular branch of the obturator nerves; and lymphatic nodes.

Name the principal muscles that keep the body erect on the thigh and give the origin and insertion of any one of them.

Gluteus maximus, medius, and minimus, tensor fasciae latae, and the two obturators. The *gluteus maximus* takes its origin from the dorsal surface of the ilium above the posterior gluteal line, the tendon of the sacrospinalis (erector spinae) muscle, the dorsal surface of the sacrum and coccyx, and the posterior surface of the sacrotuberous ligament. It is invested by the fascia lata and is inserted into the gluteal tuberosity on the femur and the iliotibial band of the fascia lata.

What muscles form the quadriceps extensor, and where is its conjoined tendon inserted?

Rectus femoris, vastus lateralis and medialis, and vastus intermedius. The tendon or *ligamentum patellae* is inserted into the tubercle of the tibia.

What muscles form the calf of the leg? Describe any one of these muscles.

Gastrocnemius and soleus. The *soleus* is a broad, flat muscle situated beneath the gastrocnemius. It *arises* by tendinous fibers from the back part of the head of the fibula and upper third of the posterointernal surface of the shaft and from the oblique line of the tibia and middle third of the inner border. The tendons of the soleus and gastrocnemius unite to form the *tendo achillis,* which is inserted into the os calcis.

Give the origin, insertion, and action of any one of the following muscles: tibialis anterior, pronator radii teres, and gracilis.

The *gracilis* arises by a linear origin from the lower half of the edge of the symphysis pubis, and for a similar distance from the adjoining part of the pubic arch. It is *inserted* on the inner side of the shaft of tibia, just below the inner tuberosity.

Action: Flexor and internal rotator of the leg and an adductor of the thigh.

Name five muscles of the back of the leg.

Gastrocnemius, plantaris, soleus, tibialis posterior, and flexor longus digitorum.

What muscles form the tendo achillis, and where is the tendon inserted?

Gastrocnemius and soleus. The tendon is inserted into the posterior tuberosity of the os calcis.

Give the names of five muscles of the male perineum.

Ischiocavernosus, sphincter urethrae membranaceae (compressor urethrae), bulbocavernosus, transversus perinei profundus, and sphincter ani externus.

Where is the sphincter urethrae membranaceae muscle?

It is between the *fascia inferior* and *fascia superior* of the *urogenital diaphragm* (triangular ligament) and surrounds the membranous urethra.

Describe the sphincter ani externus.

It is a thin flat muscle surrounding the anus and intimately adherent to the surrounding skin. It *arises* from the tip of the coccyx and is *inserted* into the central perineal point.

THE BONES

Give a general classification of bones and illustrate each class.

Long (femur, humerus); *short* (bones of the carpus and tarsus); *flat* (parietal, sternum); *irregular* (vertebra, sphenoid).

Describe the periosteum.

The membrane which surrounds bone. It consists of two layers closely united—the outer layer consists chiefly of connective tissue; the inner layer, of elastic fibers that can be separated into several layers. This membrane supplies the surface of the bone with blood and assists in its growth.

Give a brief description of the general features of the vertebral or spinal column.

Viewed from *in front* the vertebral column appears as a solid but interrupted column composed of the superimposed vertebrae, the support of the head and trunk. It is freely movable except in the lowest portion—the sacrum and coccyx. As seen *from behind* it presents three *ridges:* a central ridge formed by the spinous processes and two lateral ones formed by the transverse processes. The *vertebral grooves,* which lodge the muscles, lie between the central and lateral ridges, the floor of each groove being formed by the laminae and articular processes of the vertebrae. The movable portion includes the 7 cervical, 12 thoracic and 5 lumbar vertebrae, which are called *movable* or *true vertebrae;* and the 5 sacral and 4 coccygeal segments, which are sometimes referred to as false or fixed vertebrae. The vertebrae become heavier and stronger in the lower thoracic and lumbar regions. The *vertebral canal,* which is formed by the vertebral arches posteriorly and contains the spinal medulla and its coverings, is largest in the cervical and lumbar regions and triangular in outline. The *length* of the column is from 70 to 73 cm. in the male and about 60 cm. in the female.

The vertebral column presents *four curves* in the anteroposterior direction: there is a forward curve in the cervical region and a backward in the thoracic; the lumbar curve is a marked anterior convexity ending at the junction of the fifth lumbar vertebra with the sacrum, where the column bends sharply backward forming the prominent *sacrovertebral angle.* Finally the *hollow of the sacrum* is directed forward and mostly downward. The thoracic and sacral curves are *primary* since they exist in the fetus; the two others are *secondary* or *compensatory,* associated with the assumption of the erect posture. A slight lateral thoracic curvature is assumed to be due partly to the greater use of muscles on one side.

Give a general description of the thorax.

The thorax is a barrel-shaped, bony cage, narrower above than below, and compressed from before backward. At birth the anteroposterior and transverse diameters are about equal; in adult life the ratio is about 7 to 10; in old age it may drop to 6 to 10. The curving vertebral column projects into the thoracic cavity.

Boundaries: ANTERIOR WALL: ribs, costal cartilages and sternum.

POSTERIOR WALL: thoracic portion of vertebral column and ribs as far as their angles. On each side of the vertebral column externally it presents the *vertebral groove* of the sacrospinalis muscle.

LATERAL WALLS: costal arches.

The *ribs* run obliquely downward and forward and are not parallel to each other in front and behind, so that the intercostal spaces are considerably wider in front. The *superior aperture* of the thorax, which lies in an oblique plane directed from behind downward and forward, is bounded posteriorly (dorsally) by the first thoracic ~~cervical~~ vertebra, laterally by the first ribs, and anteriorly (ventrally) by the upper border of the manubrium. The *inferior aperture,* much wider, is bounded posteriorly (dorsally) in the median plane by the twelfth thoracic vertebra and first (horizontal) parts of the twelfth ribs; ventrally by the confluent margins of the tenth, ninth, eighth, and seventh ribs of each side meeting in front to form the *infrasternal angle* at the junction of the xiphoid process with the body of the sternum. The inferior aperture is closed by the *diaphragm,* which forms the floor of the thoracic cavity and divides it from the abdomen.

Contents: Pericardium, heart, and great vessels; the lungs and pleurae; and the contents of the mediastinal septum (space) (see page 39).

Describe the sternum, its articulations, and the important muscles attached to it.

The *sternum* is a flat, narrow bone in the median line of the front of the chest. It consists of three portions: *manubrium, body,* and *xiphoid process.* It is flattened anteriorly, concave posteriorly, broad above becoming narrowed to a point below. The average length is about 6 inches. The bone is notched at the superior angles to *articulate* with the clavicle and has seven facets on each lateral border to articulate with the seven upper costal cartilages. Important *muscles* attached to the bone are the sternocleidomastoid, pectoralis major, rectus abdominis, transversus thoracis, sternohyoid, and sternothyroid.

With what bones does the clavicle articulate?

Sternum, scapula, and cartilages of the first rib.

What is the composition of the intervertebral substance? How much of the spinal column does this substance form?

(*a*) The *intervertebral disks* or fibrocartilages are composed of laminae of fibrous tissue and fibrocartilage at the circumference, and soft, pulpy, or elastic tissue in the center derived from the nucleus pulposus. (*b*) They form about one quarter of the total length.

What is the longest bone in the body, and what are its articulations?

The *femur.* It articulates with the hip bone or os coxae (os innominatum) proximally; the tibia, and the patella distally.

Give a comprehensive description of any one of the long bones of the body.

The *femur* is the longest bone in the skeleton. It consists of a head, shaft, two trochanters, and two condyles. The *head,* which is globular, is directed upward, inward, and forward from the upper end of the shaft. A depression at the center of the upper end of the head marks the insertion of the ligamentum teres. The head is joined to the shaft by the *neck,* at an angle of about 125 degrees with the shaft in the male, less in the female.

The *great trochanter* is an irregular lateral eminence at the upper end of the shaft. It gives attachment to the gluteus medius and has a depression on the ventral surface—the *trochanteric fossa.* The *lesser trochanter* is a small, conical eminence projecting from the upper back part of the shaft. It gives attachment to the iliopsoas muscle. The intertrochanteric line and intertrochanteric crest connect these processes.

The *shaft* is triangular in the middle, broad and cylindric at the extremities. A *nutrient foramen* is situated on the dorsal surface at the junction of the middle and upper thirds. The *linea aspera* is a prominent longitudinal ridge on the dorsal surface. It has a lateral and medial lip.

The lower extremity of the femur is formed by the two *condyles* and the *intercondylic notch;* each condyle is convex anteroposteriorly and laterally. Each condyle presents a rough elevation, the epicondyle. The medial condyle is about ½ inch longer than the lateral. Above each condyle is situated a tuberosity. On the medial surface of the distal end of the femur the adductor tubercle marks the attachment of the adductor magnus.

The Skull

Mention the sutures at the vertex of the skull and state what bones they unite.

The sagittal suture unites the two parietal bones and in early life the two halves of the frontal; the lambdoid, the occipital with both parietals; the coronal, the two parietal with the frontal.

Give a general description of the skull.

The *shape* of the cranium seen *from above* varies in the relation of length to width. Elongated oval skulls are known as *dolichocephalic;* the round variety as *brachycephalic.* There are coronal, sagittal and lambdoid *sutures.* The point of junction of the sagittal and lambdoid sutures is called the *lambda;* that of the sagittal and coronal, the *bregma,* corresponding to the position of the anterior fontanelle. The summit in the sagittal suture is the *vertex.*

As seen *from the front* the frontal region is bounded below by the superciliary ridges and laterally by the temporal lines. Immediately below the superciliary ridges on each side of the bridge of the nose, formed by the two nasal bones, are the large *orbital fossae,* conical in shape, with the base directed forward and the apex toward the interior of the skull. Two openings are at the apex of the fossa; the *superior orbital fissure* (sphenoidal fissure), which transmits the third, fourth, ophthalmic division of the fifth, and sixth nerves and the ophthalmic veins; the smaller *optic foramen,* which transmits the optic nerve and ophthalmic artery. The skeleton of the face anteriorly is formed by the two *maxillae,* the two *zygomatic* (malar) bones, the two nasal bones, and the mandible. The *piriform aperture* lies below and between the orbits, its edges formed above by the free border of the nasal bones, laterally and below by the maxilla. The nasal *septum* divides the cavum nasi into two halves, and projecting into the cavity can be seen the middle and inferior *conchae* (turbinates) and the related middle and inferior *meatuses.* Below we see the upper and lower teeth embedded in the alveolar margin of the maxillae and mandible respectively. The lower dental arch is smaller than the upper. Externally, in the body of the mandible, on each side of the middle line, is seen the large *mental foramen* in line with the second premolar, the beginning of the inferior alveolar or *mandibular canal,* which ends at the *mandibular foramen* on the inner (medial) surface of the ramus about the level of the crowns of the upper teeth.

The *lateral aspect* is formed above by the frontal, parietal, and part of the occipital bones; below by the temporal and sphenoid. It presents the *temporal fossa* bounded below by the *zygomatic arch,* which is formed by the zygomatic process of the temporal and the temporal process of the zygomatic. Below are seen the mandibular fossa in front, and the opening of the external acoustic meatus behind. In the space between the condyloid process of the ramus and the mastoid process of the temporal bone may be seen, from before backward, the *styloid process* surrounded by the vaginal process and the opening of the *external acoustic meatus.* The *suprameatal triangle* of *Macewen* is a small triangular area between the posterior root of the zygoma and the superior margin of the meatus, by which the tympanic antrum can be reached by trephining.

The *posterior surface* of the skull is formed by the posterior halves of the parietal and the squamous portions of the occipital bones, united by the lambdoid suture, and by the prominent mastoid portions of the temporals. The two *parietal foramina* are placed on each side of the sagittal suture, and the point midway between them on the suture is called *obelion.* The squamous part of the occipital bone is divided into an upper and a lower portion by the *superior curved line,* the center of which constitutes the *external occipital protuberance* (*inion*). Flanking the posterior surface of the skull on either side are the mastoid processes of the temporal bone, grooved by the *mastoid notches* where the posterior bellies of the digastric muscles attach.

The *under surface* of the skull is composed of the bones of the cranium and the bones of the face. The latter comprise the hard palate, superior alveolar arch, the bodies of the maxillae and the zygomatic bones and arches, and mandible. In the middle is the *foramen magnum* lodging the medulla oblongata. The broad *occipital condyles* on the sides of the opening articulate with the atlas; in front is a plate of bone formed by the union of the body of the sphenoid and the basilar portion of the occipital bones. In the space between this plate of bone and the hard palate in front are the two *choanae* divided by the nasal septum, with the anterior and posterior *nasal spines.* The choanae are bounded laterally by the two pterygoid processes of the sphenoid, which are closely applied to the posterior extremities of the superior alveolar arch but separated from the arch by the *pyramidal process of the palate bones* (O. T. tuberosity of the palate bone). The roof and sides are formed by parts of the sphenoid.

The *hard palate,* rimmed by the alveolar arch, is made up of the palatal processes of the maxillae and the horizontal portions of the palate bones. The basilar part of the occipital bone between the body of the sphenoid in front and the anterior margin of the foramen presents the *pharyngeal tubercle* for the attachment of the pharyngeal raphe and the anterior atlanto-occipital membrane. On either side is the *foramen lacerum.* Opening into it in front is the pterygoid canal; and from behind and the lateral side is the *carotid canal,* the inferior opening of which pierces the petrous portion of the temporal bone immediately behind the angular spine of the sphenoid.

The *jugular foramen* is situated between the petrous portion in front and the jugular process of the occipital behind. The *jugular fossa* is a space of considerable size, hollowed out of the petrous portion; it contains the bulb of the internal jugular vein and the inferior petrosal sinus. Between these two structures, from before backward, the glossopharyngeal, vagus, and accessory nerves make their exit from the skull. Laterally to the jugular fossa, in line with the middle of the external acoustic meatus, is the *styloid process* of the temporal bone; the *internal jugular vein* lies close to its medial side. Behind the root of the styloid process is the *stylomastoid foramen,* which is the inferior orifice of the facial canal. Here the facial nerve makes its exit and the stylomastoid branch of the posterior auricular artery passes in.

Posteriorly to the foramen magnum the *superior nuchal line* separates the nuchal surface of the squamous portion of the occipital bone from the occipital surface. The remaining portions of the under surface of the skull are formed by the temporal bone—the squamous and tympanic portions on the two sides, with the petromastoid portion wedged in between the great wing of the sphenoid in front and the occipital behind. On either side in front are the *zygomatic arches* formed by the zygomatic processes of the temporal, and the temporal processes of the zygomatic bones.

Mention some of the more important "fixed points" on the skull. Why are they important?

Nasion: Middle of nasofrontal suture.

Glabella: A point midway between the superciliary ridges.

Bregma: Point of junction of coronal and sagittal sutures.

Vertex: Summit of cranial vault.

Obelion: A point on the sagittal suture in line with the two parietal foramina.

Lambda: Point of junction of sagittal and lambdoid sutures.

Inion: External occipital protuberance.

Gonion: Outer side of angle of mandible.

Pogonion: Most prominent point of chin.

Alveolar point or *prosthion:* Center of anterior margin of upper alveolar margin.

The object of establishing these "fixed points" is to provide for uniformity in the results of different observers in taking their measurements on the skull.

Name the foramina at the base of the skull and the structures transmitted through each.

Foramen Magnum: Transmits the spinal cord and meninges, spinal portion of accessory nerve, and vertebral arteries.

Condyloid Canal: Condyloid emissary vein (60% presence).

Hypoglossal Canal: Hypoglossal nerve, venous plexus, and small meningeal branch from ascending pharyngeal artery.

Mastoid Foramen: Emissary vein from transverse sinus, and a small branch from the occipital artery.

Stylomastoid Foramen: The facial nerve passes out, and the stylomastoid branch of the posterior auricular artery passes in.

Jugular Foramen: Jugular bulb; inferior petrosal sinus; glossopharyngeal, vagus, and accessory nerves.

Foramen Lacerum: Carotid artery, accompanied by its plexus of veins and sympathetic nerves, lies above the foramen, which in life is closed by cartilage, except for a small vein.

Carotid Canal: Internal carotid artery, sympathetic plexus, venous plexus, and meningeal branch of the ascending pharyngeal artery.

Foramen Spinosum: Middle meningeal artery and vein, and a recurrent branch (*nervus spinosus*) from the mandibular nerve.

Foramen Ovale: Mandibular division of the fifth nerve.

Foramen Rotundum: Maxillary division of the fifth nerve.

Vidian Canal: Vidian nerve.

Optic Foramen: Optic nerve and ophthalmic artery.

Superior Orbital (Sphenoidal) Fissure: Motor oculi, trochlear, abducens, and ophthalmic division of fifth nerve; ophthalmic vein.

Olfactory Foramina: Olfactory nerves.

Describe the cranial fossae, their boundaries and important contents.

These fossae have indefinite upper margins.

(1) The *anterior cranial fossa* is formed by the orbital plates of the frontal, small wings of the sphenoid, and the cranial part of the ethmoid bone. The grooves for the olfactory lobes are seen on each side of the *crista galli,* pierced by numerous foramina for the passage of the olfactory nerves to the nasal cavities. They are called the cribriform plates of the ethmoid bone.

(2) The *middle cranial fossa* is bounded anteriorly by the small wings of the sphenoid; posteriorly by the crests of the petrous ridges of the temporal bones and the top of the dorsum sellae. The floor is formed by the great wings of the sphenoid and the temporal bone. It *contains* the sella turcica; the hypophysis cerebri, the optic foramina for the passage of the optic nerves and ophthalmic arteries; the carotid groove and foramen lacerum; the foramen ovale for the transmission of the mandibular division of the trigeminal nerve; the foramen spinosum which transmits the middle meningeal vessels; the superior orbital (sphenoidal) fissure through which pass the third, fourth, ophthalmic division of the fifth, and sixth nerves and the ophthalmic vein; the foramen rotundum for the passage of the maxillary nerve; and the depression for the semilunar ganglion on the apex of the petrous portion of the temporal bone.

(3) The *posterior cranial fossa* is the largest of the three fossae. It lies posterior to the petrous crest of the temporal bone. The floor is formed by the petromastoid portion of the temporal, and parts of the sphenoid and occipital bones. It lodges the *medulla oblongata, pons,* and *cerebellum* and contains the grooves for the following sinuses: superior and inferior petrosal, occipital, and transverse.

The following foramina and openings are seen in the fossa:

Foramen Magnum: Medulla oblongata, vertebral arteries, and accessory nerves.

Opening of Canalis Hypoglossi (on each side): Hypoglossal nerves and an emissary vein.

Jugular Foramen: Lodges the jugular bulb, which joins the internal jugular vein. Here the sinuses and the glossopharyngeal, vagus, and accessory nerves make their exit from the skull.

Opening of Internal Acoustic Meatus: In the petrous portion of the temporal bone—facial and acoustic nerves and nervus intermedius, and auditory branch of basilar artery.

Mastoid Foramen: Mastoid branch of the occipital artery and an emissary vein.

Give a brief description of the bony hard palate (palatum durum).

The hard palate is formed by the two *palatal processes of the maxillae* in front and the *horizontal parts of the palate bones behind;* the front and sides are edged by the superior alveolar arch in which are embedded the sixteen teeth of the upper jaw. The posterior margin is thin and crescentic and in the median plane presents the sharp *posterior nasal spine.* The vault of the palate is concave from side to side and from before backward and varies greatly in depth. The *median palatine suture* runs the entire length of the palate from before backward and contains the *incisive foramen* in front near the incisor teeth. At the bottom of this foramen may be seen the opening of the *foramen of Stensen,* the terminal twigs for the passage of the greater palatine arteries, and the *foramina of Scarpa,* which transmit the filaments of the right and left nasopalatine nerves to the corresponding halves of the nasal cavity. The *transverse palatal suture,* which marks the union of the palatal processes of the maxillae with the horizontal portions of the palate bones, crosses the median suture at right angles and ends on each side in the *greater palatine foramen,* which is placed just medial to the root of the wisdom tooth and gives passage to the greater palatine artery and the large posterior palatine nerve. On the smooth under surface of the horizontal part of the palate bones, just behind the greater palatine foramen, is a sharp *crest* to which is attached the tensor veli palatini muscle.

Describe the pterygoid processes of the sphenoid bone.

The two pterygoid processes of the sphenoid bone, situated on each side of the choanae, consist of two plates or *laminae*—a large *lateral* and a smaller *medial* lamina with the pterygoid fossa between; in this is lodged part of the internal pterygoid muscle. The medial lamina, which separates the nasal cavity from the pterygoid fossa, has a slender hooklike extremity, which can be felt in the living behind the upper third molar. The foramen ovale and foramen spinosum are between the root of the lateral pterygoid lamina and the *angular spine of the sphenoid;* while between the base of the medial lamina and the angular spine lies the *groove for the auditory* (eustachian) *tube.*

Locate and describe the infratemporal fossa.

The infratemporal fossa forms a hollow in the side of the cranium in front of the anterior root of the zygomatic process of the temporal bone. The *lateral* (outer) wall is formed by the ramus of the mandible and its coronoid process; *anteriorly* the space is bounded by the posterior, infratemporal surface of the maxilla; the lateral pterygoid lamina represents the *medial* (inner) wall. The *pyramidal process of the palate bone* also takes part in the formation of the medial wall. The *roof* of the fossa is formed by part of the squamous portion of the temporal; the *floor,* by the lateral pterygoid lamina, which is separated anteriorly from the maxilla above the *pterygomaxillary fissure.* When the mandible is in position, the infratemporal fossa is concealed by the ramus, the medial surface of which forms the upper half of the lateral wall.

Behind the root of the lateral pterygoid lamina are the two important foramina: *ovale* and *spinosum.* The former transmits the mandibular division of the trigeminal nerve and its motor root and the accessory meningeal artery; the foramen spinosum, the middle meningeal artery and its accompanying vein.

Superiorly, under cover of the zygomatic arch, the infratemporal fossa communicates with the temporal fossa. *Medially,* on the floor of the fossa the *inferior orbital fissure* forms a communication with the orbit and transmits the zygomatic branch of the maxillary division of the trigeminal nerve; the *pterygomaxillary fissure* communicates with the *pterygopalatine fossa.*

Opening into the infratemporal fossa are the following foramina: ovale, spinosum, and mandibular; and sometimes the *foramen vesalii* transmits a vein from the cavernous sinus within the cranium to the venous plexus in the infratemporal fossa.

Name the bones of the skull.

Occipital, two parietal, frontal, two temporal, sphenoid, ethmoid, two nasal, two lacrimal, two inferior nasal conchae (turbinates), vomer, two palate, two zygomatic (malar), two maxillae, and the mandible.

What bones form the orbital cavities?

Frontal, ethmoid, sphenoid, lacrimal, maxillae, palate, and zygomatic.

What bones enter into the formation of the nasal cavities?

Frontal, sphenoid, ethmoid, two nasal, two maxillary, two lacrimal, and two palatal bones; two inferior nasal conchae; and the vomer.

Describe the nasal cavities.

They are two large, irregular cavities situated on each side of the middle line of the face. They extend from the base of the cranium to the roof of the mouth, and are separated from each other by a thin vertical *septum.* They communicate with the face by the two *nostrils,* or anterior nares, and with the pharnyx by the two *choanae,* or posterior nares.

The *roof* is formed by the following bones: nasal and frontal cribriform plate of the ethmoid, body of the sphenoid, sphenoidal process of the palate, and the ala of the vomer. The *floor* by the palatal process of the maxilla and the palate bones. The *medial wall* by a *septum* consisting of the crests of the maxillae and palate bones, the crest of the nasal, the nasal spine of the frontal, the perpendicular plate of the ethmoid, the vomer, the rostrum, and the ethmoid crest of the sphenoid. The *lateral wall* by the nasal process of the maxilla, lacrimal, ethmoid, inferior concha, vertical plate of the palate, and the medial pterygoid plate of the sphenoid.

The cavities are traversed by three longitudinal passages (meatuses): *superior,* situated beneath the superior conchae; opening into it are the sphenoid sinuses and the posterior ethmoid sinuses. The *middle* meatus is beneath the middle conchae; opening into it are the anterior ethmoid air cells, the maxillary sinus and the nasofrontal duct. The *inferior* meatus is below the inferior conchae; opening into it is the *nasolacrimal duct.*

Name and locate the accessory sinuses of the face.

Frontal, ethmoid, sphenoid, and maxillary (antrum of Highmore). The *frontal* is situated in the frontal bone beneath the superciliary ridge. The *ethmoids* are interposed between two vertical plates of bone. The lateral plate forms part of the orbit; the medial plate, part of the nasal fossa. The *sphenoid* cells are two cavities hollowed out of the interior of the body of the sphenoid bone; they are separated from one another by a bony septum. The maxillary sinus is a cavity hollowed out of the body of the maxilla.

What are the ossa suturarum or wormian bones?

In addition to the constant centers of ossification of the skull, centers are occasionally found in the course of the sutures. These form irregular, isolated bones, interposed between the cranial, and were formerly called "wormian bones."

Describe the mastoid portion of the temporal bone and name the muscles attached thereto.

The *mastoid portion* is situated at the posterior part of the temporal bone. It is perforated by the mastoid foramina. The interior contains the *mastoid cells,* lined with mucous membrane; these cells are continuous with the tympanum. The conical tip is termed the *mastoid process;* upon the medial side of the process is situated the digastric fossa, parallel and medial to which lies the occipital groove. A deep curved groove exists on the cranial surface for the lodgment of part of the transverse sinus.

The *muscles* attached to the mastoid portion are the epicranius (occipitofrontalis), auricularis posterior, sternocleidomastoid, splenius capitis, longissimus capitis, and digastric.

Describe the maxilla.

The bone consists of a hollow body and four processes. The body is cuboidal in form and hollowed out in the center into a pyramidal cavity, the *maxillary sinus.*

It has *four surfaces:* an anterior or facial that looks forward and outward;

a posterolateral or infratemporal that forms part of the zygomatic fossa; an orbital or superolateral that forms part of the floor of the orbit; and a nasal or medial that forms part of the lateral wall of the nasal cavity and the mouth.

The bone has *four processes:* zygomatic, nasal, alveolar, and palatine.

It *articulates* with the following bones: nasal, frontal, lacrimal, and ethmoid above; laterally with the zygomatic; posteriorly and medially with the palate; and on its medial side with the opposite maxilla. It supports the inferior concha and vomer.

Name the articulations of the occipital bone.

Atlas, two parietal, two temporal, and sphenoid.

With what bones does the frontal articulate?

Both parietal, both zygomatic, both nasal, both lacrimal, both maxillae, the ethmoid, and the sphenoid.

What muscles are attached to the mandible?

Masseter, buccinator, temporal, platysma myoides, quadratus (depressor) labii inferioris, triangular external and internal pterygoids, mylohyoid, geniohyoid, geniohyoglossus, and anterior belly of the digastric.

With what bones does the zygomatic articulate?

Frontal, maxilla, temporal, and sphenoid.

Mention the muscles and ligaments attached to the ramus of the jaw.

The *muscles* attached to the ramus are the masseter, internal and external pterygoid, buccinator, and temporal. The *ligaments* are the capsular and sphenomandibular of the mandibular articulation.

Describe the hyoid bone.

The hyoid is a bony arch, shaped like a horseshoe. It consists of five segments: a *body* and two great and two lesser *cornua.* It gives attachment to the sternothyroid, sternohyoid, stylohyoid, digastric, mylohyoid, geniohyoid, and geniohyoglossus muscles; and the following ligaments: stylohyoid, thyrohyoid, and the thyrohyoidean membrane.

Upper Extremity

Name the bones articulating with the humerus.

Scapula, radius, and ulna.

With what bones does the radius articulate?

Humerus, ulna, navicular (scaphoid), and lunate (semilunar).

Name and describe the arrangement of the carpal bones.

They are placed in two rows of four each. Enumerating from the radial to the ulnar side, with the palm upward, proximal row: navicular, lunate, os triquetrum (cuneiform), and pisiform. Distal row: greater multangular (trapezium), lesser multangular (trapezoid), os capitatum (os magnum) and os hamatum (unciform).

Describe the bones of the hand with their divisions and articulations.

The bones of the hand are divided into three classes: carpal, metacarpal, and phalanges. There are *eight carpal bones* (see previous question). The carpals articulate with each other; the navicular and lunate with the radius; the os triquetrum with the interarticular disk or triangular interarticular cartilage between it and the ulna; the greater and lesser multangular, capitate, and os hamatum with the metacarpal bones. The *five metacarpal* bones articulate with those just described, the first row of phalanges, and with each other. The first row of *phalanges* articulates with the metacarpals and the second row of phalanges; the second row with the first and third rows. There are fourteen phalanges. The thumb has only two phalanges.

The Vertebral Column

Give in language or by drawing the normal curvatures of the spinal column, and describe a typical cervical vertebra.

The curves are *cervical, thoracic, lumbar,* and *sacrococcygeal.* The convexity is forward in the cervical, backward in the thoracic, forward in the lumbar, and backward in the coccygeal. The line of gravity of the trunk passes through the cords of these curves.

A typical cervical *vertebra* consists of a small body, diverging roots of the vertebral arches (pedicles), and laminae, a bifid spinous process, and bifid transverse processes, which are grooved on the upper border. Each transverse process is perforated at its base by a foramen for the vertebral artery. The neural foramen is relatively large.

Give the number of the cervical vertebrae and mention the marked characteristics of such of these as are in any way peculiar.

Seven.

The *atlas* or first cervical vertebra is formed by two lateral masses joined by an anterior and posterior arch; the anterior arch presents a facet on its posterior surface for articulation with the *dens* (odontoid process) of the *epistropheus* (axis). Upon the upper surface of each lateral mass is an articular facet, which articulates with the occipital condyles; on the inferior surface the facet looks downward and articulates with the epistropheus or second cervical vertebra.

The *epistropheus* has, surmounting the body, the dens with a facet on the anterior surface for articulation with the atlas and another facet on the posterior surface for the transverse ligament. The toothlike dens is roughened at the apex by the alar or check ligaments.

The *seventh,* or *vertebra prominens,* resembles the other cervical vertebra, except that the spinous process is longer and ends in a single broad tubercle.

Describe one of the vertebrae.

Each vertebra consists of two essential parts, an anterior solid segment or *body* and a posterior segiment or *arch.* The arch is formed by two *roots* or *pedicles* and two *laminae,* which support seven *processes,* two superior and two inferior articular, two transverse (extending laterally from the pedicles), and a spinous process, the continuation posteriorly of the laminae.

What is a cervical rib?

The costal element of the transverse process of the seventh or sixth cervical vertebra occasionally develops as a complete or rudimentary free rib. Cervical ribs may be unilateral or bilateral and may augment the scalenus syndrome (pressure on vessels and nerves).

The Pelvis

What bones make up the pelvis? Give the gross anatomy of the bony pelvis.

Two ossa coxae or hip bones, sacrum, and coccyx. The pelvis is formed by the union of the hip bones in front and the sacrum behind. It is divided into *small* and *large* by a plane passing through the *promontory* of the sacrum and the *iliopectineal line.* The part above this plane (the large pelvis) is formed by the expanding iliac bones. The part below (the small pelvis) is bounded in front by the body and rami of the pubis, posteriorly by the sacrum. Between the sacrum and the spine of the ischium is the *greater sciatic notch.*

What is the chief difference between the male and female pelvis?

In the *female* pelvis the bones are lighter, the muscular impressions less marked, the iliac fossa is broader, and the anterior superior spines are more widely separated. The *pelvic inlet* is larger and more nearly circular, the projection of the sacrovertebral angle is less. The concavity of the pelvis is shallower and wider, the outlet is larger, the coccyx more movable, and the pubic arch wider. The obturator foramen is triangular and smaller than in the male, in whom it is oval.

Describe the bones forming the ossa coxae.

The hip bone or *os coxae,* the largest of the flat bones, consists of three parts: the *ilium, ischium,* and *os pubis.*

The *ilium* has a curved crest extending from the anterior superior, to the posterior, spine. The medial surface forms the *iliac fossa* limited below by the *iliopectineal line;* the lateral surface is marked by the anterior, posterior, and inferior *gluteal lines.* The anterior inferior spine gives attachment to the rectus femoris muscle and the *iliofemoral* (Y) *ligament;* it is situated below the superior spine. The ilium forms part of the *small pelvis* and two fifths of the *acetabulum.* It fuses with the os pubis and ischium at the eighteenth to the twentieth years. It articulates with the sacrum posteriorly.

The lower and posterior part is formed by the *ischium,* the body of which forms the lower two fifths of the acetabulum and part of the small pelvis. On the medial and posterior border, on a level with the lower edge of the acetabulum, the iliac spine separates the *greater* from the *lesser sciatic notch.* Below is the *tuberosity of the ischium,* the lowest part of the pelvis, from which the *ramus ascends* to join the inferior ramus of the pubis and form the *obturator foramen.*

The *pubis* has two *rami,* superior and inferior, which fuse to form the body and partly bound the obturator foramen. It presents two surfaces: the posterior forms the anterior wall of the small pelvis and supports the bladder; the anterior surface gives attachment to the gracilis, adductor longus, and adductor brevis, and part of the obturator externus muscles. From the upper border or *crest* arise the rectus abdominis and pyramidalis muscles. Laterally the crest terminates in a pointed process, the *pubic tubercle* (pubic spine), to which is attached the inguinal ligament. The pubic portion of the iliopectineal line passes along the superior ramus, which is grooved on its under surface for the obturator vessels and nerves. The *arcuate* (subpubic) *ligament* is attached to the lower border of the inferior ramus.

Describe the acetabulum.

This is a cup-shaped depression for the lodgment of the head of the femur formed by the os pubis, ischium and ilium. It is surrounded by a prominent, uneven rim which has a deep notch—the *acetabular notch*—on its inferior surface, continuous with a circular depression at the bottom of the cavity, to which the *ligamentum teres* or round ligament is attached.

The Lower Extremity

When (i.e., at what time of life) do the epiphyses join the shaft of the femur?

The lesser trochanter about the eighteenth year, the great trochanter about the nineteenth year, and the lower epiphysis from the twentieth to the twenty-second year.

Mention the muscular and the ligamentous attachments of the patella.

Muscles: quadriceps femoris tendon; *ligaments:* the anterior (ligamentum patellae) and the two collateral patellar.

What forms the medial malleolus of the ankle joint?

The lower end of the tibia.

What forms the lateral malleolus?

The lower outer end of the fibula.

Describe the bones of the foot, giving their divisions and articulations.

The *tarsal bones* are the calcaneus or os calcis, talus or astragalus, cuboid, navicular or scaphoid, and first, second, and third (internal, middle, and external) cuneiform bones; the *metatarsal* bones are five in number; the *phalanges* number fourteen. The *astragalus* articulates with the tibia, fibula, os calcis, and scaphoid. The *os calcis* articulates with the astragalus and cuboid. The *scaphoid* articulates with the astragalus and three cuneiform bones. The *cuneiform* bones articulate with the scaphoid proximally, and with the first, second, third, and fourth metatarsal bones distally. The metatarsals articulate with the three cuneiform and the cuboid behind, and with each other laterally, and with the phalanges in front. The first row of *phalanges* articulates with the metatarsals and the second row of phalanges; the second row, with the first and third rows. The great toe has only two phalanges.

What metatarsal joint is the weakest in the arch of the foot?

The talonavicular.

What bone forms the heel and with what does it articulate?

The calcaneus. It articulates with the talus and cuboid.

The Joints

Differentiate synarthrosis, amphiarthrosis, and diarthrosis, giving an example of each.

Synarthrosis is an immovable joint consisting of two bones placed edge to edge with little or no fibrous tissue intervening; example: lambdoid suture. *Amphiarthrosis* is a joint permitting of slight motion, made up of two bones with an intervening fibrocartilaginous plate or disk, and held together by ligaments; example: joints formed by bodies of the vertebrae and intervertebral disk. *Diarthrosis* is a freely movable joint consisting of two or more bones with articular surfaces covered with hyaline cartilage, lined with synovial membrane, and surrounded by ligament; example: hip joint.

Describe the shoulder joint.

The shoulder joint is an *enarthroidal* (ball-and-socket) joint formed by the head of the humerus and the glenoid fossa of the scapula. It is lined by synovial membrane which communicates with several of the numerous surrounding bursae. The *ligaments* are the *fibrous stratum of the articular capsule* (capsular ligament), which surrounds the margin of the glenoid fossa and is inserted into the upper part of the neck of the humerus; the transverse humeral, coracohumeral, the glenoid fossa or labrum glenoidale, and the long tendon of the biceps. The nerves to the joint are the suprascapular, axillary, and subscapular. The arteries are the *transverse scapular* (suprascapular) and the anterior and posterior circumflex.

Describe the elbow joint, name the ligaments, and give their attachments.

The elbow joint is a *ginglymus* or hinge joint formed by the *trochlear surface* of the humerus articulating with the semilunar or *radial notch* of the ulna and the *capitulum* of the distal end of the humerus articulating with a shallow *depression* on the head of the radius. The articulating surfaces are covered with cartilage. The joint is surrounded by a *capsular ligament* which is attached proximally to the humerus above the articular surface; distally, it is attached to the olecranon and coronoid processes of the ulna and the neck of the radius. The *radial collateral* ligament radiates from the lateral condyle to the outer side of the neck of the radius. The *ulnar collateral* ligament is attached proximally to the medial condyle; distally to the medial side of the shaft and olecranon process of the ulna. The *annular ligament of the radius* surrounds the neck of the radius and is attached to the margins of the radial notch.

What structures enter into the distal radio-ulnar articulation?

The triangular articular disk (fibrocartilage), annular ligament, interosseous membrane, and anterior and posterior radio-ulnar ligaments.

Describe the wrist joint.

It is formed by the radius and triangular articular disk proximally, and the navicular, lunate, and cuneiform bones distally. (The ulna is separated from the cuneiform bone by the triangular articular disk, hence is excluded from the wrist joint.) The ligaments are the *volar* and *dorsal radiocarpal, lateral radiocarpal,* and *medial ulnocarpal.* The *movements* are flexion, extension, radial abduction, ulnar abduction, and circumduction.

Name the ligaments of the hip joint.

The ligaments are the capsular, pubocapsular, iliofemoral, ischiocapsular, teres, labrum glenoidale (cotyloid ligament) and transverse.

Describe the hip joint.

The hip joint is an *enarthroidal diarthrosis* or ball-and-socket joint. The joint consists of the head of the femur resting in the *acetabulum* and surrounded by the *capsular ligament.* The acetabulum is incomplete below for entrance of vessels and nerves. Both the head and the acetabulum are covered by articular cartilage. The capsular ligament is assisted by the following *ligaments:* Y or iliofemoral, labrum glenoidale, transverse, pubocapsular, and ischiocapsular. The joint has the following *movements:* flexion, extension, adduction, rotation, and circumduction. The *arteries* supplying the joint are derived from the obturator, sciatic, medial circumflex, and gluteal. The *nerves* supplying the joint are derived from the sacral plexus, and the sciatic, obturator, accessory obturator, and femoral nerves.

Describe the Y or iliofemoral ligament.

It is a divided band of fibers extending obliquely across the front of the hip joint intimately connected with the capsular ligament (fibrous stratum). The Y is inverted. It is attached *above* to the anterior inferior spine of the ilium and diverges *below* into two bands: one passes downward, to be *inserted* into the lower part of the intertrochanteric line; the other passes downward and lateral to the upper part of the same line.

(*a*) Discuss the structures and arrangements that give strength to the hip joint. (*b*) In what position of the thigh is the strength of hip joint decreased to the greatest degree so as to favor dislocation?

(*a*) Owing to the necessity for strength and stability in maintaining the erect posture, in supporting the weight of the trunk, and in locomotion, the range of movements at the hip joint is more limited than at the shoulder. The joint is provided with stout ligaments, which do not permit the head of the femur to move away from the acetabular articular surface except to a very limited extent and which prevent excessive movement in any direction. The *labrum glenoidale,* which forms part of the acetabular cavity, encircles the head of the femur and holds it within the cavity. The action of the powerful muscles that act on the femur or, when the thighs are fixed, on the trunk in flexion, extension and rotation, is controlled and restricted by the various ligaments of the hip joint. The two most important are the *capsular ligament* and the *iliofemoral* or Y ligament so-called, which is really part of the longitudinal fibrous stratum of the capsular. The Y ligament is attached above (proximally) to the anterior inferior iliac spine and distally to the intertrochanteric line of the femur. Its effect when rendered tense is to maintain the erect posture and prevent excessive extension or "dorsiflexion" of the trunk.

The strong *transverse ligament* bridges the acetabular notch and is attached chiefly to the postero-inferior margin of the acetabulum. The *pubocapsular ligament,* extending from the superior ramus of the pubis and adjoining parts to the neck of the femur and blending with the lower part of the capsule and distal attachment of the iliofemoral, acts as a check on *abduction,* which is also interfered with by locking the neck of the femur against the edge of the acetabulum. Excessive *adduction* is prevented by tension of the upper band of the Y ligament and upper part of the capsular. *Rotation medially* (toward the front) is checked by tension of the *ischiocapsular ligament* and posterior part of the capsule; *lateral rotation* (toward the back) by the upper limb of the Y ligament. The function of the *round ligament,* which is not always present, is still in doubt. It is probably rendered tense during the act of walking, at the moment when the body is balanced on the top of the femur. In the erect posture it lies relaxed in the acetabular cavity.

(*b*) The capsular ligament is thickest and strongest at its superoanterior aspect and weakest in its inferior portion where it is attached to the labrum glenoidale and transverse ligament. Hence the region of the acetabular notch is a weak spot in the joint and *dislocation* is most likely to occur in *abduction,* when the head of the femur is brought into relation with this weak region.

Describe the structure of the knee joint.

The joint is a *ginglymus* or hinge joint, and consists of three articular surfaces, one between each condyle of the femur and the tibia and also one between the femur and the patella. The surfaces between the femur and the tibia are separated at the periphery by two *semilunar menisci* of fibrocartilage, wedge-shaped in cross section. The joint is surrounded by a *capsular ligament,* strengthened by an anterior and posterior and a fibular and tibial collateral ligament. Within the joint are the following *ligaments:* anterior and posterior cruciate, transverse, and coronary. The *blood supply* is derived from the arteria genu suprema (anastomotica magna) and the popliteal, anterior tibial, and lateral circumflex arteries. The *stratum synoviale* or synovial membrane of the knee joint is the largest in the body. The *nerve supply* is derived from the obturator, femoral, common peroneal, and tibial nerves. Its *actions* are flexion, extension, and slight rotation with the joint flexed.

Name the bones that form the ankle joint and give their relations.

The *tibia, fibula,* and *talus.* The talus rests in a cavity formed by the lower end of the tibia above, by the malleolus of the tibia medially, and by the lower end of the fibula laterally.

Name the ligaments of the ankle joint.

Capsular, anterior, posterior, deltoid, and calcaneofibular.

What is connective tissue? Where in the body is connective tissue found?

By the term "connective tissue" we mean a number of tissues derived from mesoderm which possess the following feature in common: that they serve the general purpose in the animal economy of supporting and connecting the tissues of the frame. The principal forms are *white fibrous, yellow elastic,* and *areolar.* It is distributed throughout the body and forms the sheaths of muscles, blood vessels, and nerves, also ligaments, tendons, etc.

RESPIRATORY SYSTEM

Describe the gross anatomy of the larynx.

The *larynx* is the valve of the chest and the organ of voice. It lies in the upper part of the neck, in front of the pharynx, between the trachea and the base of the tongue. The framework is formed by the thyroid, cricoid, arytenoid, and epiglottic cartilages with two minor paired cartilages, the cuneiform and the corniculate. It is lined with mucous membrane. The paired ventricular folds, the false cords, lie above the paired laryngeal ventricles, and the vocal folds, the true vocal cords, lie below, at about the midpoint of the thyroid cartilage. The opening bounded by the vocal folds is the *glottis,* the narrowest part of the upper air passages and a site of lodgment of foreign bodies. The numerous bundles of muscle fibers act as abductors (muscles of respiration) or adductors (muscles of phonation). The superior aperture is wide in front and narrow behind; it is bounded above by the *epiglottis.* The cavity of the larynx extends from the superior aperture to the lower border of the cricoid cartilage.

The *blood supply* is derived from the superior and inferior thyroid arteries. The *superior laryngeal nerve* pierces the thyrohyoid membrane and supplies sensation to the interior of the organ; the *recurrent laryngeal* is the motor nerve to all the muscles except the cricothyroid, which is supplied by the superior laryngeal.

Describe the cartilages of the larynx.

Thyroid, cricoid, epiglottis, two arytenoid, two cuneiform, and two cornicula. The *thyroid* consists of two alae united in front at an acute angle; the upper border is attached to the hyoid bone by the thyrohyoid membrane, the lower border articulates with the cricoid on each side and is connected to the cricoid by the cricothyroid membrane anteriorly. The *cricoid* is ring-shaped and united to the thyroid as given above. Its lower border is connected to the upper ring of the trachea by a fibrous membrane. The *arytenoids* are pyramidal, situated at the upper border of the lamina of the cricoid cartilage. Each *articulates* with the cricoid and corniculate cartilages, and gives attachment to the vocal folds and the following muscles: cricoarytenoid, arytenoid, and thyroarytenoid. The *epiglottis* is placed behind the tongue, in front of the superior opening of the larynx; the superior portion is free; the inferior portion is connected to the angle between the thyroids by the thyro-epiglottic ligament. The *corniculates* surmount the apices of the arytenoid cartilages. The *cuneiform* are contained in the aryteno-epiglottidean folds.

Give the anatomy of the vocal folds.

The *vocal folds* are placed below the ventricular folds; they extend from the angle between the alae of the thyroid cartilages to the vocal processes of the arytenoid cartilages. The folds are sharp and prominent; the investing mucous membrane has stratified squamous epithelium.

What structures are severed in tracheotomy?

Skin and superficial and deep cervical fasciae. The sternothyroid muscle is separated from its fellow, and the pretracheal fascia and tracheal rings are divided. In dire emergency the opening into the air passage is made through the cricothyroid membrane.

Describe the pleura.

The *pleura* is a serous membrane covering the lungs (pulmonary, investing, or visceral layer), thoracic surface of the diaphragm, the inner surface of the wall, and the mediastinum (the parietal layer).

Give the divisions of the mediastinum, their boundaries, and their contents.

The mediastinum is the space between the mediastinal portions of the two pleural sacs. It is bounded ventrally by the sternum and dorsally by the vertebral column. It is divided into *four* portions, as follows:

(*1*) *Superior or Cranial:* That part which lies above the level of the pericardium.

BOUNDARIES:

Ventrally—manubrium.
Dorsally —first four thoracic vertebrae.
Below —imaginary plane from inferior border of manubrium to inferior border of fourth thoracic vertebra.
Laterally—mediastinal pleurae.

CONTENTS:

Ascending aorta, aortic arch, and the three great arteries which spring from it.
Innominate veins and lower part of superior vena cava.

Trachea, esophagus, and thoracic duct.
Phrenic, vagi, cardiac, and left recurrent nerves. Thymus.

(2) *Ventral or Anterior:* That part which lies between the pericardium dorsally and the body of the sternum ventrally.

BOUNDARIES:

Ventrally—sternum.
Dorsally —pericardium.
Laterally—pleurae.
Below —diaphragm.
Above —imaginary plane through sternal ends of fourth costal cartilages.

CONTENTS:

A few lymph nodes and lymph vessels and areolar tissue.

(3) *Middle Mediastinum:* The wide part which lies below the superior mediastinum and contains the pericardium and the phrenic nerves and accompanying vessels.

(4) *Dorsal or Posterior Mediastinum:* That part which lies behind (dorsal to) the pericardium.

BOUNDARIES:

Above —fourth thoracic vertebra.
Ventrally—pericardium and vertical part of diaphragm.
Dorsally —last eight thoracic vertebrae.
Laterally—mediastinal pleurae.

CONTENTS:

The dorsal mediastinum is practically a continuation of the dorsal part of the superior mediastinum and contains many of the same structures. In addition: the descending thoracic aorta with the aortic intercostal arteries and the azygos (azygos major) and the hemiazygos (and the accessory hemiazygos) veins, the thoracic duct, the esophagus, and the two vagus nerves.

Describe the trachea.

The *trachea* is a cartilaginomembranous cylindrical tube, slightly flattened dorsally. It is kept patent by a series of *cartilaginous rings,* which are deficient dorsally. It begins, above, at the inferior border of the cricoid, opposite the sixth cervical vertebra; from this point it extends downward through the lower part of the neck into the superior mediastinum, ending opposite the fifth thoracic vertebra by dividing into right and left bronchi. The caliber is variable; it exhibits a slight dilatation about the middle, and another at the bifurcation. The length is about 4 inches.

Give an anatomic description of the bronchi.

They are two branching systems derived from the right and left main stem bronchi. Their cartilaginous character persists until the diameter of 1 mm. is reached, when they become entirely membranous. They are lined with ciliated columnar epithelium. The *right bronchus* is wider, about 1 inch shorter, and takes a more vertical course than the left. The *blood supply* is derived from the aorta or from the first intercostal. The veins empty into the pulmonary veins directly and the azygos system by way of the bronchial veins and the lymphatics into the bronchial nodes. The *nerves* are branches of the vagus and sympathetic.

Describe the lungs.

The lungs are the essential organs of respiration. They are two in number, one in each side of the chest. Each lung is conical in shape and presents for examination an *apex* and *a base; three surfaces:* diaphragmatic, mediastinal, and costal; and *two borders,* a ventral or anterior and an inferior. The curving diaphragmatic surface is also called *the base.* Each lung is divided into *two lobes* by a long fissure that begins dorsally about 2½ inches below the apex and extends downward and forward (ventrally) to the lower part of the anterior border. The upper lobe of the right lung is partially subdivided by a short fissure, forming the wedge-shaped *middle lobe of the right lung.* Each lobe is further subdivided into bronchopulmonary segments. Typically, but not always, each segment has its own blood supply, which makes possible the surgical removal of part of a lobe. The right upper lobe has three segments, the middle two, and the lower five. On the left side, the upper lobe has four segments grouped into upper and lower divisions of two each. The lower lobe has four segments. The *root* of the lung is situated above the middle of the mediastinal surface and attaches the lung to the mediastinal wall. It is formed by the bronchus, the two pulmonary veins, the pulmonary artery, pulmonary and bronchial arteries and veins, pulmonary nerves, and lymphatics. The mediastinal surface is hollowed out in adaptation to the pericardium. Above and dorsal to the pericardial hollow is the *hilus,* where the bronchus and the blood vessels, nerves, and lymph vessels enter and leave the lung.

Structure: The lung is composed of an external serous coat (visceral layer of the pleura), subserous areolar tissue which invests the surface of the lung, and the parenchyma. The parenchyma is composed of *lobules* closely connected together by interlobular areolar tissue. Each lobule is composed of one of the ramifications of a bronchial tube with the terminal *air cells,* and the ramifications of the pulmonary and bronchial vessels, lymphatics, and nerves. The lungs receive *blood* through the bronchial arteries for their own *nutrition,* and venous blood through the pulmonary artery for *aeration.* The bronchial veins empty on the right side into the vena azygos; on the left, into the vena hemiazygos. The *nerve supply* is derived from the vagus and the anterior and posterior pulmonary plexuses of the sympathetic system.

ALIMENTARY TRACT

Name the subdivisions of the alimentary canal and give the name and location of the various glands found in the small intestine.

Mouth, pharynx, esophagus, stomach, duodenum, jejunum, and ileum; ascending, transverse, descending, iliac, and sigmoid or pelvic colon; rectum and anus.

The *glands* in the small intestine are: duodenal ("Brunner's"), found in the duodenum; the glandulae intestinales or intestinal follicles ("crypts of Lieberkühn"), found in the whole length of the small and large intestine. The noduli lymphatici solitarii and noduli lymphatici aggregati (Peyer's patches), found in all parts of the small intestine but most numerous in the ileum, are, strictly speaking, not glands but "nodes."

Describe the tongue.

The *tongue* is a large mobile mass composed chiefly of muscular tissue and covered by mucous membrane. It occupies the floor of the mouth and forms the anterior wall of the oral pharynx. The sense of taste resides chiefly in its modified epithelium. The tongue is also an important organ of speech and assists in the mastication and deglutition of the food.

Describe the tonsils and name some of the arteries which supply them with blood.

The *tonsils* are placed between the glossopalatine and pharyngopalatine arches (anterior and posterior pillars) in the sinus tonsillaris or tonsillar recess, close to the base of the tongue. They vary greatly in size and shape. Their surface is irregular and marked by numerous depressions leading into *crypts* in the substance of the tonsil; the crypts are surrounded by follicles of lymphoid tissue. The *arteries* that supply the tonsils are the dorsalis linguae, ascending palatine, tonsillar branches of the facial, descending palatine of the internal maxillary, and the ascending pharyngeal branch of the external carotid.

Describe the pharynx.

The *pharynx* is the upper portion of the digestive tube. It communicates with the mouth, larynx, nasal cavities, auditory (eustachian) tubes, and esophagus. It extends from the base of the skull to the sixth cervical vertebra (lower border of cricoid cartilage). It is divided into the nasal, oral, and laryngeal pharynx (pars nasalis, pars oralis, pars laryngea). The pharynx is a musculomembranous sac about 5 inches in length, broader transversely than anteroposteriorly. In the nasal pharynx are situated the *pharyngeal tonsils* and the *orifices of the auditory tubes;* the space posterior to the tubes in the lateral wall is called the recessus pharyngeus or lateral recess (*fossa of Rosenmüller*). The oropharynx is the portion between the soft palate and the superior aperture of the larynx; it contains the *faucial tonsil.* The laryngeal pharynx is that portion situated behind the larynx; on either side it contains the *recessus* (*sinus*) *piriformis.* The *blood supply* is derived from the internal and external maxillary arteries. The *nerve supply* is derived from the ninth and tenth nerves and the sympathetic system.

Name the seven openings into the pharynx.

Larynx, mouth, esophagus, two auditory tubes, and two choanae.

Describe the esophagus as to (a) location, (b) dimensions, and (c) arterial supply.

(*a*) The esophagus extends from the cricoid cartilage to the cardiac end of the stomach. In the neck it lies between the trachea and the vertebral column and longus colli muscle; in the lower part of the neck it inclines to the left, having on each side the common carotid artery and the lateral lobe of the thyroid gland. The recurrent laryngeal nerves ascend between the esophagus and the trachea. In the thorax the esophagus lies at first slightly to the left; after passing behind the aortic arch it descends in the posterior mediastinum along the right side of the aorta to the diaphragm, where it passes forward before entering the abdomen and joining the stomach.

(*b*) *In length* it usually measures about 10 inches (25 cm.). Its *breadth,* where the tube is widest, varies between ½ inch (13 mm.) in the empty contracted condition and 1 inch or more (25 to 30 mm.) in the fully distended state.

(*c*) The *arterial supply* is derived from the inferior thyroid, thoracic aorta, and left gastric and left inferior phrenic arteries.

The Stomach

Describe the stomach, give its average size, attachments, regional location, gross structure, and blood supply.

The *stomach* is irregularly piriform in shape, with a wide or *cardiac end* directed backward and to the left, and a narrow *pyloric end* that extends to the right to join the duodenum. In addition to its two ends, the stomach presents for examination the following parts: two *curvatures, greater* and *lesser,* which separate the *anterior* and *posterior surfaces;* and two *orifices,* the esophageal orifice or *cardia* and the pyloric orifice or *pylorus.*

Size: Probably no organ in the body varies more in *size,* within the limits of health, than the stomach. Consequently it is difficult, perhaps impossible, to arrive at a correct estimate of its size and capacity. The length in the fully distended condition is about 10 to 11 inches (25 to 27 cm.), and its greatest diameter not more than 4 to 4½ inches (10 to 11 cm.). The *capacity* of the stomach in the average state rarely exceeds 40 ounces, or 1 quart.

Attachments: The stomach is *attached* to the spleen by the *gastrosplenic ligament* (omentum) and to the diaphragm by the gastrophrenic ligament; the lesser curvature is attached to the under surface of the liver by the *hepatogastric ligament,* part of the lesser omentum. It is *located* in the left hypochondriac, epigastric, and part of the right hypochondriac regions. The stomach is composed of *four coats*—namely, from without inward: (1) serous or peritoneal, (2) muscular, outer longitudinal, middle circular, and inner oblique, (3) submucous, and (4) mucous membrane.

Blood Vessels: The arteries of the stomach are all derived ultimately from the celiac artery. The left gastric from the celiac, the right gastric from the hepatic, the right gastro-epiploic from the gastroduodenal, the left gastro-epiploic and vasa brevia from the splenic.

Describe the pyloric orifice of the stomach.

The *pylorus* is the aperture through which the stomach communicates with the duodenum. It is marked externally by a circular constriction, the *sulcus pyloricus* or *pyloric constriction,* and internally by a prominent thickening of the wall. The pyloric valve is produced by a special development of the circular muscular fibers known as the *pyloric sphincter.*

Into what, and how far from the pyloric orifice of the stomach, does the ductus choledochus normally open?

The ductus choledochus or *bile duct* (common bile duct) empties into the duodenum (descending portion) upon its concave side, 3 or 4 inches below the pyloric orifice.

The Liver

Mention the ligaments, fissures, and lobes of the liver.

The *ligaments* are seven in number, falciform (suspensory), round, coronary, right and left triangular, venous ligament of Arantius (obliterated ductus venosus), and the omentum minus. The fissures are: porta hepatis, fossa venae umbiliacalis (fissure for the round ligament—obliterated umbilical vein), fossa of the gallbladder, and fossa venae cavae (fissure of the inferior vena cava).

The lobes are: the left, right, quadrate, and caudate (spigelian) with its processus caudatus (caudate lobe).

Locate and briefly describe the gallbladder.

It is a pear-shaped, fibromuscular *receptacle for the bile.* The fundus, the under surface of the body, and the neck of the gallbladder are covered with peritoneum. The *length* is from 3 to 4 inches (7.5 to 10 cm.), *capacity* 8 to 12 drams (30 to 45 cc.). The gallbladder lies in a fissure on the under surface of the liver, with the fundus, its most dilated portion, projecting slightly beyond the anterior border at the ninth costal cartilage. It is lined with cylindrical epithelium and marked by numerous rugae. It empties into the cystic duct.

The Pancreas

Give the gross and the topographic anatomy of the pancreas.

The *pancreas* is a compound racemose gland from 6 to 8 inches long by 1 inch wide (17.5 cm. by 2.5 cm.). It is composed of a number of *lobules,* each lobule consisting of an ultimate branch of the pancreatic duct lined with columnar epithelium and surrounded by a capillary network of blood vessels. The *pancreatic duct* (Wirsung) extends the whole length of the gland and opens into the middle of the descending duodenum with the bile duct; the *accessory duct* (Santorini), when present, opens into the duodenum about 1 inch above the former. The *head,* or right extremity, is embraced by the concavity of the duodenum, the *tail* rests on the spleen above the left kidney, the *body* is covered by the ascending layer of the transverse mesocolon and posterior surface of the stomach; the superior mesenteric artery and vein, portal vein, inferior vena cava, aorta, the left renal vessels, left suprarenal gland, and left kidney separate it from the posterior abdominal wall.

The islands of Langerhans, small interlobular masses composed of pale cells with fine granules, have no ducts but are in close relation with the capillary endothelium surrounding them.

The *blood supply* is received from the splenic and superior and inferior pancreaticoduodenal arteries. The *nerves* are derived from the celiac plexus through the hepatic and splenic plexuses.

The Intestines

Describe the greater omentum.

The greater omentum consists of *four peritoneal surfaces,* two anterior and two posterior. The middle layers constitute the wall of the *bursa omentalis* (lesser sac), the two external belong to the greater peritoneal cavity. Up to the age of 2 years there is a cavity between the two inner surfaces. The omentum resembles a four-cornered curtain. It hangs down from the greater curvature of the stomach in front of the small intestine; posteriorly it is fused with the transverse colon. Its vessels, the *vasa epiploica,* are derived from the right and left gastroepiploica; the *nerves,* from the celiac plexus.

Describe the mesentery.

When the peritoneum on the vertebral column reaches the anterior surface of the superior mesenteric vessels it follows them down to the loops of small intestine, surrounding all the jejunum and ileum, but not the duodenum, and returns to the vertebral column. This peritoneal reflection is called the *mesentery* and serves to support the intestines. It has a right upper and a left lower layer, between which are the mesenteric arteries and veins, lacteals, lymphatics, nerves, and fat. The origin of the two layers is called the *root* of the mesentery; it extends from the left side of the body of the second lumbar vertebra to the right sacroiliac articulation.

Locate and describe the valvula coli or ileocecal valve.

It is formed by two horizontal semilunar folds of mucous membrane at the *termination of the ileum* in the cecum. The valve opens toward the large intestine and guards against reflux from the large into the small bowel; the mucous folds are reinforced by circular muscle fibers.

The Small Intestine

Give a general description of the small intestine.

Three divisions of the small intestine are described: (1) *Duodenum,* the first part, immediately succeeding the stomach. (2) *Jejunum,* the upper two fifths of the small intestine proper (*intestinum tenue mesenteriale*), about 8 feet in length. (3) *Ileum,* measuring about 12 feet. It opens into the large intestine by the *valvula coli* (ileocecal valve).

The small intestine presents the following distinctive features: the presence of *villi* distributed throughout the jejunum and ileum; *plicae circulares; intestinal glands; solitary* and *aggregated lymph nodes.* These glands and lymph nodes are lodged in the submucosa and tunica mucosa.

Mesentery: The small intestine, with the exception of the duodenum, is attached to the posterior abdominal wall by the mesentery, a broad fan-shaped fold of peritoneum, which also conveys vessels and nerves to the intestine. It has two borders: the mesenteric or attached border, also called the *root of the mesentery,* and the *free border* opposite to the former. The *root,* 6 or 7 inches in length, is attached to the posterior abdominal wall from the left side of the second lumbar vertebra to the right sacroiliac articulation. The free border, about 20 feet long, contains the intestine within its two layers. The mesentery contains in addition (*a*) the branches of the superior mesenteric vessels and mesenteric nerve plexus; (*b*) the mesenteric lymph nodes, numbering from 40 to 150; and (*c*) fatty connective tissue.

Blood and Nerve Supply: Duodenum —branches of the gastroduodenal and superior mesenteric arteries. Jejunum and ileum—branches of the superior mesenteric arteries. Drainage by the superior mesenteric vein, which joins with the splenic to form the portal vein. The nerves of the small intestine derive from the solar plexus.

Mention some of the special features of the different portions of the small intestine.

Duodenum: In shape it resembles a horseshoe and is about 11 inches long. It has no mesentery. It joins the jejunum by the *duodenojejunal flexure,* which is attached above by a thin band of unstriped muscle to the celiac artery and the left crus of the diaphragm. This is known as the *m. suspensorius duodeni* (Treitz). The tela submucosa contains the *glandulae duodenales* (glands of Brunner) which are much like the pyloric glands of the stomach. The *villi* covering the tunica mucosa are broader and shorter than in the jejunum and ileum.

Jejunum: This is wider than the ileum. Plicae circulares are well developed. Aggregated lymph nodes are few and small. The villi are shorter and broader than in the ileum.

Ileum: The prominent feature is the presence of the *aggregated lymph nodes* (Peyer's patches), which are numerous and well developed. Plicae circulares are absent or very small.

Diverticulum Ilei (*Meckel's Diverticulum*): This is a short protrusion from the lower part of the ileum, about 2 inches long, occurring in a little over 2 per cent of bodies examined. It is usually found about 2¾ feet from the valvula coli, opposite the termination of the superior mesenteric artery. The end is usually free, but may become attached to surrounding structures and is then subject to strangulation, inflammation, and infection (*diverticulitis*). The abnormality is due to the persistence of the proximal part of the vitelline duct.

Locate and describe the cecum.

The *cecum* lies in the right iliac fossa, above the lateral half of the inguinal ligament, and is that part of the large intestine situated below the *valvula coli* (ileocecal valve). It has longitudinal bands, sacculations, and three coats, like every other part of the large intestine. It is usually completely covered with peritoneum. The length is 2½ inches, breadth about 3 inches.

In *shape* it presents a wide, lopsided sac, the wider lower portion or *fundus* directed downward, the opposite end upward and laterally, continuing into the ascending colon. The small intestine joins the cecum on the medial aspect, from which also the *vermiform process* (appendix) comes off, 1 to 1½ inches lower down.

There are three types of cecum: (1) *Fetal*—conical and nearly symmetrical; the process arises gradually from the lower end.

(2) *Infantile*—more asymmetrical; the process arises more abruptly.

(3) *Adult*—as described above. The original (lower) extremity, with the vermiform process springing from it, is displaced and hidden away behind the medial side of the fundus.

Describe and give the anatomic relation of the processus (appendix) vermiformis.

It is a wormlike tubular outgrowth that springs from the medial and posterior surface of the cecum, about 1 inch below the ileocecal orifice. It may point in any direction, but usually in one of the following: over the brim of the pelvis into the pelvis, upward behind the cecum, upward and inward toward the spleen. The size varies: it is usually about 3½ inches long and ¼ inch thick. The lumen also varies, being largest in the young. It is covered with peritoneum, which forms the mesenteriolum processus vermiformis (mesoappendix) at the lower border. The structure is the same as that of the large intestine—namely, serous, muscular (longitudinal and circular), submucous, and mucous layers. It also contains lymphoid nodules.

The Large Intestine

Give a general description of the intestinum crassum (large intestine).

The *large bowel* or *colon* begins on the right side, about 2½ inches below the ileocecal junction and ends at the anal orifice. It surrounds the small intestine in an arched manner so that the latter lies within the concavity of the curve. The length is 5 to 5½ feet; the greatest width, at the cecum, is about 3 inches; beyond this point it diminishes gradually to about 1½ inches in the descending division. It is distinguished from the small intestine by (*a*) the presence of three longitudinal bands—the *taenia coli*—running along its surface; (*b*) by the fact that its walls are sacculated; and (*c*) by the presence of the *appendices epiploicae,* small peritoneal processes projecting from its serous coat. On the interior surface the sacculations appear as rounded pouches—*haustra*—separated by crescentic folds—*plicae semilunares coli*—corresponding to the creases in the exterior. The inner surface is smooth, has no villi, but presents the openings of numerous *intestinal glands* and *solitary lymph nodes.*

The *right* (hepatic) flexure joins the ascending and transverse colons. The *left* (splenic) flexure similarly forms the connecting part between the transverse and descending colons; it is attached to the abdominal wall by the *phrenicocolic ligament.*

The *blood supply* is furnished by branches of the superior and inferior mesenteric arteries and by the three hemorrhoidal arteries (rectum). The veins drain into the portal vein.

Mention the divisions of the large intestine.

(1) *Cecum.*

(2) *Ascending Colon:* In the right lumbar region, extending from the cecum to the under surface of the liver. Length from 5 to 8 inches. Partially covered with peritoneum.

(3) *Transverse Colon:* An irregular curved loop passing across the abdominal cavity from the right to the left flexure. Length about 20 inches. It is completely covered with peritoneum except for the first few inches of the posterior surface.

(4) *Descending Colon:* Running down the left side from the left flexure to the rectum. The following parts are described:

DESCENDING COLON: From the flexure to the iliac crest; 4 to 6 inches.

ILIAC COLON: From the crest of the ilium to the superior aperture of the pelvis; 5 or 6 inches, variable.

PELVIC COLON: A large loop usually found in the pelvis. Length about 16 inches, very variable. The iliac and pelvic portions together form the colon sigmoideum (sigmoid flexure).

(5) *Rectum:* Terminal portion of the large intestine, from the pelvic colon to the anal canal, which opens on the surface as the *anal orifice.*

The descending colon, iliac colon, and rectum are partially, the pelvic colon is completely, covered with peritoneum and has a mesentery, the *pelvic mesocolon.*

The Rectum

Locate and describe the rectum.

The *rectum* begins at the termination of the pelvic mesocolon, at the level of the third sacral vertebra, and ends where the bowel pierces the pelvic floor, which is a point 1½ inches in front of, but at a lower level than, the tip of the coccyx. It first descends along the front of the sacrum and coccyx, following along the curve of these bones; beyond the coccyx it rests on the pelvic floor. The rectum resembles the large bowel, except that it is only partially covered with peritoneum. It is formed by the same coats and has longitudinal bands but no mesentery. The *plicae trans-*

versales recti (Houston's valves) are infoldings of the lateral wall caused by the shortness of the anterior and posterior longitudinal bands. If the *anal canal* is included as part of the rectum, then there are the *columnae rectales* (columns of Morgagni), which are vertical folds of mucous membrane. If a probe is passed downward between two adjacent columnae rectales, it will catch in a small crescentic fold which joins the lower ends of the columns; these folds are the *anal valves.* The usual length of the rectum is from 5 to 6 inches.

State (*a*) the nerve supply and (*b*) the blood supply of the rectum.

(*a*) Sympathetic branches from the inferior mesenteric, and hypogastric plexuses. Cerebrospinal fibers from the second, third, and fourth sacral nerves; also from the inferior hemorrhoidal branches of the pudendal.

(*b*) Superior hemorrhoidal, branch of inferior mesenteric, the principal artery of the rectum; two middle hemorrhoidals, branches of hypogastric or internal pudendal; inferior hemorrhoidals, branches of internal pudendal; and branches of middle sacral artery.

Describe the ischiorectal fossa and its contents.

The *fossa* is situated between the lower end of the rectum and the tuberosity of the ischium. The space is *triangular* in shape; the base, which is directed toward the surface of the body, is formed by the integument of the ischiorectal region; the *apex* is directed upward and corresponds to the point of division of the obturator fascia and the anal fascia. The *medial boundary* is formed by the anal fascia covering the levator and sphincter ani muscles; the *lateral boundary,* by the tuberosity of the ischium and obturator fascia covering the obturator internus muscle. The space is limited *in front* by the line of junction of the superior and deep perineal fasciae; *behind* by the margin of the gluteus maximus muscle and sacrotuberous ligament.

In the outer wall of the fossa the internal pudendal vessels and nerve are enclosed in a sheath of obturator fascia (Alcock's canal). The ischiorectal space is filled with adipose tissue and crossed anteriorly by the perineal vessels and nerve, in the middle by the inferior hemorrhoidal vessels and nerve, posteriorly by the fourth sacral nerve.

With reference to the alimentary tract: (*a*) Where is stratified epithelium found? (*b*) What parts have the heaviest musculature? (c) Where is it smallest in caliber and where largest? (*d*) Name all the parts that are freely suspended and all parts tightly bound to the body wall. (e) Name the parts that are completely or almost completely covered with peritoneum, and those which are only partially covered. (*f*) What region receives the most abundant glandular secretion?

(*a*) Mouth and tongue, oral part of pharynx, esophagus, lower part of rectum.

(*b*) Jejunum, cecum, rectum, and anal canal.

(*c*) At pylorus; next to pylorus the esophagus. Largest in caliber in stomach; next to stomach in ascending colon.

(*d*) Esophagus (loosely connected by areolar tissue); cecum; jejunum except at its beginning; ileum except at its ending; transverse colon (beyond its attachment by a short mesentery to duodenum and pancreas, it hangs down in front of small intestine); pelvic colon.

Parts bound to body wall: pharynx, duodenum, descending colon, iliac colon, and rectum. (The ascending colon is attached to the iliacus and quadratus lumborum muscles and to the right kidney; the stomach to the liver, spleen, transverse colon and diaphragm.)

(*e*) Stomach, jejunum, ileum, cecum, transverse colon, pelvic colon. Partly covered: duodenum, ascending and descending colon, iliac colon, and rectum.

(*f*) Ileum and stomach.

THE PERITONEUM

Locate and name the apertures in the walls of the abdomen and the structures passing through them.

The *subcutaneous inguinal* (external abdominal) *ring* is situated above and to the outer side of the os pubis in the aponeurosis of the external oblique muscle; it transmits the *funiculus spermaticus* (spermatic cord) in the male and the round ligament in the female. The *abdominal inguinal* (internal abdominal) *ring* is situated in the transversalis fascia midway between the anterior superior spine of the ilium and the spine of the pubis; it transmits the funiculus spermaticus in the male and the round ligament in the female. Openings in the diaphragm: the *aortic opening* is between the crura of the diaphragm and transmits the aorta, vena azygos, and thoracic duct. The *foramen venae cavae* (quadrate foramen) is in the right lobe of the central tendon and transmits the inferior vena cava. The *esophageal opening* is in the muscular substance behind the central tendon; it transmits the esophagus and nerves.

Describe the peritoneum.

The peritoneum is a serous membrane, forming a closed sac, the layer covering the walls being called the *parietal,* and that reflected over the viscera, the *visceral* layer. It is coated with a layer of flattened *endothelium,* its attached surface being connected with the subjacent parts by the subperitoneal areolar tissue or fascia. For convenience, the peritoneum is divided into the *great sac* (greater cavity) and the *bursa omentalis* (lesser cavity).

The great sac covers the upper anterior portion of the liver and the stomach in front and above, descends over the ileum, forming the anterior layer of the *great omentum,* the under layer of the mesocolon, the *mesentery,* and reflections upon and between the rectum, the uterus in the female, and the bladder, then lines the anterolateral abdominal walls, to reach, from the under surface of the diaphragm, the upper surface of the liver.

The bursa omentalis starts from the diaphragm behind, passes over the lobe of the liver, then covers the back and under surface of the stomach, forms the inner layer of the great omentum, passes over the colon, completing the mesocolon, and thence passes over the pancreas and great vessels to line the posterior abdominal wall.

The two cavities communicate through the *foramen epiploicum* (foramen of Winslow).

Name the abdominal viscera wholly covered with peritoneum; those partially covered.

(*a*) Cecum, appendix, jejunum, and ileum.

(*b*) Liver, spleen, kidneys, suprarenals, colon, duodenum, pancreas, stomach, rectum, uterus, ovary, and bladder.

Locate and describe the spleen.

The *spleen* is a soft, spongy, very vascular ductless gland, about 5 by 3 by 2 inches in length, breadth, and thickness and weighs from 6 to 10 ounces. It is situated in the left hypochondrium, between the fundus of the stomach, kidney, diaphragm, and colon and is attached to the diaphragm and stomach by folds of peritoneum. The *hilus* is a vertical fissure on the concave surface for the entrance of the vessels and nerves. *Structure:* The gland is covered almost entirely by peritoneum, and is encased in a fibro-elastic *capsule* which is reflected inward at the hilus to form the framework of the organ. This framework supports the *splenic pulp* comprising connective-tissue cells, pigment granules, red blood cells in all stages of disintegration, and malpighian bodies. The *noduli lymphatici lienales* (malpighian bodies) are masses of lymphoid tissue surrounding the splenic capillaries.

THE ABDOMEN

Name the regions of the abdomen.

Right and left hypochondrium; epigastrium; right and left lumbar, umbilical; and right and left iliac regions; and pubic region or hypogastrium.

Where in the topography of the abdomen is the sigmoid flexure located? The processus vermiformis?

(*a*) In left iliac and hypogastric regions. (*b*) In right iliac region.

What anatomic parts are normally found in the left hypochondriac region?

Fundus of stomach, spleen, tail of the pancreas, left flexure of the colon, and the upper part of the left kidney.

What is contained in the right hypochondriac region?

Portion of the liver, the gallbladder, the right flexure of the colon, and the upper part of the kidney.

What is found in the right iliac region?

Last part of the ileum, the cecum, and the vermiform process.

Describe the inguinal ligament, naming its anatomic relations and uses as a surgical guide.

The *inguinal ligament* (Poupart) is the lower border of the aponeurosis of the external oblique muscle. The ligament extends from the anterior superior spine of the ilium to the spine of the os pubis; from this latter point it is reflected downward filling in the medial angle of the femoral canal. The reflected portion is called *ligamentum lacunare* (Gimbernat's ligament). The lower border is continuous with the fascia lata of the thigh. The medial part of the ligament forms the floor of the *inguinal canal* and the lateral pillar of the *subcutaneous inguinal ring*, also the medial boundary of the *femoral canal.* Beneath the ligament are found, from without inward, the lateral cutaneous and femoral nerves and the femoral artery and vein. It is the guide in inguinal hernia and in ligation of the external iliac and femoral arteries.

Describe the abdominal inguinal ring.

The ring is an *oval opening* in the transversalis fascia midway between the anterior superior spine and the pubis, ½ inch above the inguinal ligament. The ring is *bounded* above and laterally by the transversalis muscle, below and medially by the inferior epigastric vessels. It *transmits* the spermatic cord in the male and the round ligament in the female. It is covered by infundibuliform fascia.

Describe the inguinal canal.

It is a flat-sided passage in the lower part of the inguinal region, extending between the abdominal and subcutaneous inguinal rings; the *floor* is formed by the transversalis fascia and the conjoined tendon, the *roof* by the external oblique muscle. It is about 1½ inches long in the adult. It contains the funiculus spermaticus in the male and the round ligament in the female.

Give the surgical anatomy of femoral hernia.

The hernia descends through the femoral ring carrying with it the *femoral septum,* passes through the femoral canal (the medial channel of the femoral sheath), and is directed forward through the *fossa ovalis* in the fascia lata and pierces the *fascia cribrosa* to reach the groin.

The *coverings* of a femoral hernia are, from without inward, skin, superficial fascia, fascia cribrosa, femoral sheath, femoral septum, extraperitoneal tissue, and peritoneum.

What is (a) the processus vaginalis peritonei, (b) canal of Nuck, (c) the urachus?

(*a*) A small diverticulum of the peritoneal cavity sometimes remaining from the descent of the testis.

(*b*) Similar diverticulum in the female related to the round ligament.

(*c*) After the separation of the cloaca to form the bladder and rectum, the portion of the allantois that lies in the body of the embryo, between the apex of the bladder and the umbilical orifice, is gradually converted into a fibrous cord —the *urachus*.

THE URINARY SYSTEM

The Kidneys

Give the location and describe the anatomic structure of the kidneys.

The kidneys are situated in the lumbar region and rest upon the psoas major and quadratus lumborum muscles. The upper end of the left kidney reaches as high as the upper border of the eleventh rib, the upper end of the right as high as the lower border of the eleventh rib. Each is capped by a suprarenal body. The kidney is surrounded by a *capsule* or *tunica fibrosa* and a perirenal connective tissue containing fat (*capsula adiposa*); it is supplied by the renal artery and drained by the renal vein and lymphatics. The nerves are derived from the renal plexus of the sympathetic system.

The kidney is bean-shaped. The notch on the inner border is called the *hilus* and leads into a depression or cavity known as the *sinus*. The *ureter* begins in the sinus and the vessels and nerves enter or leave by way of it. The interior consists of a connective-tissue parenchyma, supporting vessels, and uriniferous tubules. It is subdivided into the *cortex* and the *medulla*. The cortex contains the *glomeruli* (coiled-up blood vessels) and some of the tubules; the medulla consists of *pyramids* (malpighian or medullary) made up of parallel collecting tubules, which terminate upon the apex of the pyramid and pour the urine into the calices of the *pelvis of the kidney*. The uriniferous tubules begin around a glomerulus as a closed extremity—*capsula glomeruli* (capsule of Bowman)—and pass tortuously through the cortex (loop of Henle), terminating in one of the collecting tubules found in the *pyramid*.

Describe the arteries and veins passing to and from the kidneys.

The *arteries* spring nearly at a right angle from the sides of the aorta below the superior mesenteric branch; the right is longer than the left and passes behind the inferior vena cava. Each divides into four or five branches before entering the hilus. The *veins* pass out of the hilus, transversely across the abdomen to the inferior vena cava; the left is the longer, and passes in front of the aorta; it also receives the left spermatic vein. Relations of structures at the hilus from before backward: vein, artery, ureter.

Describe the renal blood circulation.

The arterial blood enters the sinus through the hilus by means of the renal artery, the branches of which pass between the malpighian pyramids to the corticomedullary junction, where they form transverse branches that, in turn, send arterioles into the cortical and medullary portions, forming glomeruli in the former and plexuses around the uriniferous tubules in the latter. The veins collect the blood from the cortex and medulla and form corticomedullary veins, which pass through the medullary portion between the pyramids and leave the kidney through the sinus as the renal vein.

Give the relations of the right kidney.

It extends *from the eleventh rib* nearly *to the iliac crest;* the *anterior* surface is in relation with the right lobe of the liver, descending portion of the duodenum, and right flexure of the colon; the *posterior* surface rests on the right crus of the diaphragm. The transversalis aponeurosis separates it from the quadratus lumborum muscle. It is capped by the suprarenal capsule.

Give the course and relations of the ureters in the male and female.

The course of the *ureter* is divided into the abdominal and pelvic portions. The *abdominal* portion, about 5 inches in length, is directed downward and slightly inward and lies upon the psoas major muscle. On both sides the internal spermatic or ovarian vessels pass in front and the genitofemoral nerve behind; on the right side the descending duodenum lies in front of the upper part, and the line of attachment of the mesentery crosses it lower down. On the left side the line of attachment of the mesentery of the pelvic colon crosses the ureter. The *pelvic portion* is about 4 inches in length and passes downward on the lateral wall of the pelvis. In its course within the pelvis the ureter lies in front of the hypogastric artery and crosses the medial aspect of the obturator nerve and vessels and the obliterated umbilical artery. About the level of the ischial spine the ureter bends somewhat inward above the fascia of the pelvic floor to reach the bladder. In this position it is crossed by the *ductus deferens.* A little further on in its course the ureter is in relationship with the upper end of the *vesicula seminalis* and passes in front of it to the bladder wall. When the right and left ureters reach the bladder they are about 2 inches apart. They pierce the bladder wall very obliquely and are embedded within its muscular tissue for nearly ¾ inch. They finally open into the bladder by two small slitlike apertures, which are valvular and prevent a backward passage of fluid from the bladder. *In the female* the ureter, near its termination, passes beneath the lower part of the broad ligament and lies to the lateral side of the cervix uteri and upper part of the lateral wall of the vagina.

The Bladder

Locate and describe the bladder.

The *bladder* is a musculomembranous sac, situated in the pelvis behind the pubis and in front of the rectum in the male, and behind the pubis and in front of the cervix and upper part of the vagina in the female. It varies in size and shape with age; in infancy it is conical, in the adult oval. The *summit* is connected to the anterior abdominal wall by the urachus and obliterated umbilical arteries. The *body* is in relation inferiorly with the triangular ligament, symphysis pubis, and obturator internus muscle. The abdominal surface is covered by peritoneum; the *base* rests on the rectum in the male, the cervix and anterior vaginal wall in the female; the *neck* is constricted and continuous with the urethra. The neck is surrounded by the *prostate* in the male. The true *ligaments* are two anterior, two lateral, and a superior (urachus); the false are two posterior, two lateral, and a superior. The interior surface of the bladder is lined by mucous membrane; at the base is a triangular area with the apex at the urethra and the other angles at the orifices of the ureters (*trigonum*).

Structurally, the bladder consists of an external fibrous layer partially covered by peritoneum, a muscular layer (external and internal longitudinal, middle circular), and submucous and mucous layers.

The *ureters* open into the lower and under part of the bladder, about half an inch from the median plane.

Minutely describe the relations of the peritoneum to the bladder.

The superior surface of the empty bladder is covered by peritoneum, which leaves it along the lateral borders to reach the pelvic wall (*lateral false ligament*). In front it is reflected upon the urachus to reach the anterior abdominal wall (*superior false ligament*); when the bladder is empty this reflection lies below the symphysis pubis; when full, it may reach a level 2 inches above the symphysis. Posteriorly it is reflected upon the rectum in the male, the uterus in the female (*posterior false ligaments*); this reflection posteriorly does not alter to any extent during distention of the bladder.

What portion of the bladder is uncovered by peritoneum?

The anterior wall, which is separated from the symphysis pubis by the prevesical space (Retzius) and the base of the bladder.

Describe the male urethra and state its divisions.

The *male urethra* is a channel about 8 inches in length, leading from the bladder to the external urethral orifice at the extremity of the glans penis. The course of the urethra from the internal urethral orifice to the external meatus is S-shaped. It is customary to divide the urethra into the *prostatic, membranous,* and *cavernous portions.* The first part of the urethra lies within the pelvic cavity and has an almost vertical course as it traverses the prostate. Turning forward, the urethra passes below the pubic arch and pierces the *inferior fascia of the urogenital diaphragm.* Leaving the pelvic cavity, the urethra enters the *bulbus urethrae,* where the latter is attached to the triangular ligament, and throughout the rest of its course it lies on the erectile tissue of the *corpus cavernosum* and glans penis. The common ejaculatory ducts and prostatic ducts open into the prostatic urethra; the bulbo-urethral (Cowper's) glands into the bulb. Numerous minute glands (glandulae urethrales) pour their secretion into the urethra.

Describe the female urethra as to (a) location, (b) dimensions, and (c) structure.

(*a*) The *female urethra,* after leaving the bladder, follows a slightly curved course downward and forward, below and behind the lower border of the symphysis pubis. As it leaves the pelvis, the urethra pierces the *urogenital diaphragm.* The portion that lies between the deep and superficial layers of the diaphragm is surrounded by the fibers of the sphincter urethrae membranaceae (compressor urethrae) muscle. It passes from the urogenital diaphragm to the urethral orifice in the tissues below the symphysis and above the vagina.

The external orifice is placed between the *labia minora,* immediately in front of the opening of the vagina, about 1 inch below and behind the *clitoris.*

(*b*) Except during the passage of urine the surfaces of the urethra are in apposition. The length is about 1½ inches.

(*c*) The wall of the urethra is thick and contains much fibrous tissue; beneath this is found a *muscular layer* that is continuous with the bladder and is composed of layers of inner circular and outer longitudinal smooth muscular fibers. Beneath this layer is the *vascular layer,* composed of blood vessels and elastic fibers; this layer is lined by epithelium, transitional in the upper part and scaly in the lower. Numerous mucous glands open into the urethra.

THE GENITAL SYSTEM

Female Genitalia

Relate the differences between a virgin uterus and the uterus of a multipara.

The uterus of a multipara is larger, the cavity more marked, the *plicae palmatae* are almost effaced, and the external os is irregular or stellate instead of being a smoothly outlined slit. The cervix is smaller in proportion to the uterus than in the virgin.

Describe the broad ligaments of the uterus and their anatomic relations.

The *broad ligaments* are double folds of peritoneum extending from the sides of the uterus to the lateral walls of the pelvis; with the uterus they form a septum across the pelvis. They are reflected anteriorly upon the bladder, posteriorly upon the rectum. Between the two layers are found the uterine (fallopian) tubes, epoophoron (parovarium or organ of Rosenmüller), uterine and ovarian arteries and veins, and lymphatics. The ovaries are attached to the posterior surface near the lateral wall of the pelvis.

Describe the uterine (fallopian) tubes and give their relations.

They are a pair of ducts which convey the ova from the *folliculi ovarici vesiculosi* (graafian follicle) of the ovary to the uterus. They are about 4 inches long and are enclosed in a fold of peritoneum called the *mesosalpinx* (a portion of the broad ligament). Each tube consists of three portions—an *isthmus* or the portion that joins the uterus, an *ampulla* or middle portion, and an *infundibulum* or outer portion. The external opening is called the *abdominal ostium* and is surrounded by *fimbriae.*

The tube consists of an outer serous, a middle muscular (superficial longitudinal, deep circular), a submucous, and an inner mucous coat that is continuous with the lining of the uterus.

Locate and describe the ovaries.

They are two flattened, ovoid bodies suspended by their anterior margins from the posterior surface of the broad ligaments, below the uterine tubes. They are attached by their medial extremities to the uterus by the utero-ovarian ligaments (ligaments of the ovary); by their lateral ends to one of the fimbriae.

Structure: An ovary consists of a number of folliculi oophori vesiculosi embedded in the ovarian stroma. The ovary is covered by a serous layer derived from the peritoneum, but differs from that structure in consisting of columnar cells instead of endothelium. It is attached to the broad ligament by a short mesentery, the *mesovarium.* The stroma consists of connective tissue with numerous spindle cells and abundant blood vessels. The follicles are minute vesicles from $\frac{1}{100}$ inch in diameter to even $\frac{1}{20}$ inch after puberty. Microscopically they have an external fibrovascular coat (*theca folliculi*) and an internal coat lined by a layer of nucleated cells, the *membrana granulosa* or *stratum granulosum;* these cells are heaped up around the ovum at that part of the follicle nearest the ovarian surface to form the *discus proligerus.* The graafian follicle contains a transparent albuminous fluid surrounding the ovum.

Describe the vagina.

The *vagina* is a cavity about 3 inches in length, open at its lower end, and communicating above with the cavity of the uterus. The cavity is directed downward and forward, describing a slight curve, which is convex backward. The vagina is wider in the middle than at either end, and normally its anterior and posterior walls are in contact. In transverse section the lower part is usually an H-shaped cleft, the middle part a simple transverse slit, while the lumen of the upper portion, into which the *cervix* projects, is more open. Since more of the posterior than of the anterior part of the cervix projects into the vagina, a deeper recess is formed between the posterior vaginal wall and the cervix than in front or laterally. The *anterior* vaginal wall is shorter than the *posterior,* the former being about 3 inches in length, the latter about 3½ inches. At its lower end the vagina opens into the *rima pudendi* or *urogenital cleft,* the opening being situated behind the orifice of the *urethra* and *clitoris* and between the *labia minora.* The opening is partly closed in the virgin by a thin crescentic or annular fold called the *hymen,* torn fragments of which persist around the opening as the *carunculae hymenales* after the fold has been ruptured.

Male Genitalia

What anatomic parts are involved in the descent of the testes?

In early fetal life the *testis* rests on the lower pole of the kidney and is connected with the inguinal region by the *gubernaculum testis.* A diverticulum of the peritoneum (*processus vaginalis*) goes downward and inward through the abdominal inguinal ring, inguinal canal, and subcutaneous inguinal ring, into the scrotum and into the testis, to which it is attached. It lies in front of the spermatic cord. The diverticulum is gradually obliterated except for the tunica vaginalis testis. The connection with the peritoneum closes.

What are the vesiculae seminales?

They are a pair of hollow, sacculated structures, about 2 inches in length, placed in front of the rectum and posterior to the bladder. They are really diverticula of the ductus deferentes and consist of outer fibrous, intermediate muscular, and inner mucous layers. In function they secrete seminal fluid and may store spermatozoa.

Name the component parts of the funiculus spermaticus or spermatic cord.

Ductus deferentes; cremaster muscle; external spermatic and testicular arteries, and arteria deferentialis; genital branch of genitofemoral nerve, ilio-inguinal nerve; pampiniform plexus of veins; and lymphatics.

Describe the structure of the prostate and give its anatomic relations.

The *prostate* is enclosed in a fibrous *capsule.* The substance is reddish brown and consists of *muscular* and *glandular* tissue. The muscular tissue consists of a circular layer immediately beneath the *capsule* and around the urethra; also scattered bundles through the gland. The glandular tissue consists of numerous follicular pouches opening by small excretory ducts into the prostatic urethra. The prostate is situated immediately in front of the neck of the bladder and surrounds the commencement of the urethra. It is in the pelvic cavity, behind and below the pubis, and posterior to the deep perineal fascia. The posterior surface rests upon the rectum.

Name in their order the structures between the cutaneous surface of the perineum and the mucous membrane of the bladder at the prostatic plane.

Skin, superficial fascia, inferior hemorrhoidal vessels and nerves, bulbocavernosus, transversus perinei muscle and artery, deep perineal fascia, levator ani, sphincter urethrae membranaceae (compressor urethrae), and membranous and prostatic portions of the urethra.

THE SKIN

What are the layers of the skin?

The skin has three layers. The outer epithelial layer is the epidermis. It extends into the hair follicles and glands. The next layer is dense connective tissue, the true skin, derma, or corium. This layer is extremely vascular. The subcutaneous layer is loose connective tissue and fat.

Describe a hair follicle.

The follicle is an invagination of the epidermis and corium which, in the case of large hairs, extends into the subcutaneous tissue. Each hair follicle has a *duct of a sebaceous gland* opening into it. The portion of the follicle derived from *corium* consists of a fibrous sheath of external longitudinal, and internal circular, connective-tissue fibers. The parts of the follicle derived from the *epidermis* are named the inner and outer *root sheaths.* The bottom of the hair follicle is indented by a vascular papilla derived from the corium and capped by the *bulb* or expanded part of the hair root.

THE EYE

How is the eye supplied with blood?

By the ophthalmic artery, a branch of the internal carotid, which gives off the ciliary and arteria centralis retinae branches.

Name the humors of the eyeball.

Aqueous and vitreous.

Describe the eyeball and give its parts.

The *bulb of the eye* (eyeball) is not quite spherical. It is perforated by the optic and ciliary nerves and the ciliary and central artery of the retina. At the junction of the anterior segments the globe is pierced by the anterior ciliary artery. The eyeball is composed of the segments of two spheres, an anterior, transparent, *corneal segment,* and a posterior, opaque, *scleral portion,* the union of the two parts being indicated externally by a slight groove, the *sulcus sclerae.* The central points of the anterior and posterior curvatures constitute respectively the *anterior* and *posterior poles.* The sagittal and transverse diameters are nearly equal, usually about 24 mm.; the vertical diameter is about 23.5 mm. The eyeball consists of three concentric tunics, contained within which are three transparent refracting media. The three tunics are: (1) an outer fibrous coat, the *sclerocornea,* consisting of an opaque posterior part, the *sclera,* and a transparent anterior portion, the *cornea;* (2) an intermediate vascular, pigmented, and partly muscular tunic, the *tunica vasculosa oculi,* comprising from behind forward the *choroid,* the *ciliary body,* and the *iris;* (3) an internal nervous tunic, the *retina.* The three refracting media are named from before backward: the *aqueous humor,* the *crystalline lens,* and the *vitreous body.*

Describe each of the tunics of the eye and the different parts of each.

The *outer tunic* consists of the sclera and cornea. The *sclera* is a firm, opaque membrane, consisting of bundles of fibrous tissue closely interlaced. The sclera forms the posterior five sixths of the outer tunic. It is pierced on the nasal side of the posterior pole by the optic nerve. At the equator are four openings for the exit of veins called *venae vorticosae.* The *cornea* is transparent, and consists of bundles of fibrous tissue enclosing corneal spaces in which are lodged corneal corpuscles. The cornea is richly supplied by sensory nerve fibers and is nonvascular. It consists, from before backward, of the following strata: (1) a layer of stratified epithelium; (2) an anterior elastic lamina; (3) the substantia propria; (4) a posterior elastic lamina; and (5) a layer of endothelium.

The *middle tunic* consists of the *choroid,* the *ciliary body,* and the *iris.* The *choroid* intervenes between the sclera and the retina, reaching as far forward as the *ora serrata* of the latter. The choroid is dark brown and is pierced posteriorly by the optic nerve. It is firmly attached to the sclera and thicker behind than in front. Its outer surface is flocculent and is connected to the sclera by the ciliary vessels and nerves and by the loose *lamina fusca.* Its inner surface is smooth and adheres to the outermost or pigmented layer of the retina. The *ciliary body* connects the choroid to the circumference of the iris and presents the following three zones: (*a*) *orbicularis ciliaris,* (*b*) *ciliary process,* and (*c*) the *ciliary muscle.* The *iris* forms a contractile diaphragm in front of the lens and is pierced a little to the nasal side of its center by an almost circular aperture, the *pupil.* The peripheral border of the iris is directly continuous with the ciliary body and, through the medium of the *ligamentum pectinatum iridis,* with the posterior elastic lamina of the cornea. The space between the cornea and the crystalline lens is divided by the iris into two portions containing the aqueous humor, called the *anterior* and *posterior chambers.*

The *retina* is the innermost tunic, and is made up of nerve cells and fibers representing the expansion of the optic nerve. The layers from within outward are: (1) layer of nerve fibers; (2) layer of nerve cells; (3) inner molecular, (4) inner nuclear, (5) outer molecular, and (6) outer nuclear layers; (7) layer of rods and cones; and (8) layer of pigmented epithelium. The *macula lutea* is the point of most acute vision and is located to the temporal side of the optic disk. The retina is supplied by the *arteria centralis retinae,* a branch of the ophthalmic, and drained by the central vein of the retina into the ophthalmic vein.

What are the ciliary processes in the eye? Where are they placed, and what is their average number?

They are formed by the folding inward of the choroid at its anterior margin, and are received between the foldings of the suspensory ligament of the lens. They are attached to the ciliary muscle and arranged in a circle behind the iris. They average 70 in number.

Describe the iris, giving its blood and nerve supply.

The *iris* is a thin, circular, perforated, contractile curtain, suspended behind the cornea and in front of the lens in the aqueous humor. It is the anterior portion of the middle ocular tunic and is formed of radiating and circular muscular fibers, nerves, veins, arteries, lymphatic spaces, and fibrous stroma. Anteriorly, it is covered by a layer of polyhedral cells which are continuous with *Descemet's membrane.* The *pupil* is the opening in the iris and is placed slightly to the nasal side of the center. In the fetus the pupil is occluded by a membrane until about the eighth month. The *ligamentum pectinatum* is a reticular tissue connecting the iris and cornea. The *uvea,* a layer of purplish-hued pigment cells on the posterior surface, is continuous with the pigment layer of the *ciliary processes.* The circular muscle contracts the pupil; the radiating fibers dilate it. The *arteries* are branches of the long and anterior ciliary. The *veins* empty into the ciliary process and anterior ciliary veins. The *nerves* are branches of the third, fifth, and sympathetic, through the long and short ciliary; third going to the sphincter (circular fibers), sympathetic to the sphincter (dilator fibers), and fifth, nerve of common sensation.

Describe the crystalline lens and state what tissues are in contact with it and how.

The *lens* is a transparent biconvex body, more convex posteriorly than anteriorly. It is enclosed in a *capsule* and consists of lens fibers derived from epithelial cells (ectoderm), arranged in layers, which are softer in consistency near the surface (*cortex*), and more compact at the center (*nucleus*). It is nonvascular in the adult; the hyaloid artery supplies it in the fetus. The lens is lodged in a depression in the vitreous where it is retained by the suspensory ligament attached to the ciliary body. The margin of the pupil rests upon its anterior surface.

Describe the lacrimal apparatus.

The *lacrimal gland,* which secretes the tears, is lodged in a depression at the lateral and upper angle of the orbit. It pours the tears on the conjunctiva at the lateral angle of the lids. The tears pass over the eyeball and enter the *puncta lacrimalia,* which are situated on the lacrimal papillae, on the medial end of the lids, at the lateral extremity of the *lacus lacrimalis.* From the puncta the tears pass through the two lacrimal ducts to the *lacrimal sac.* The lacrimal sac is lodged in a deep groove formed by the *lacrimal bone* and maxilla. The sac empties into the *nasolacrimal duct,* which is a membranous canal about ¾ inch in length; it in turn empties into the *inferior meatus* of the nose. The opening into the nose is guarded by the plica lacrimalis or valve of Hasner.

THE EAR

What are the parts of the ear?

The ear consists of three parts, the external ear, the middle ear, and the internal ear.

Describe the external ear.

The external ear consists of the auricle and the external auditory canal. The outer two thirds of the canal has a cartilaginous wall, the inner one third is bony. The external ear includes the outer surface of the drum head. Sebaceous and ceruminous glands are in the canal skin.

Describe the middle ear.

The middle ear is the air chamber extending from the inner surface of the drum head to the promontory of the opposite wall. It is connected with the pharynx by the auditory tube (eustachian) and extends upward into the epitympanum. There is a connection with the tympanic antrum from which the mastoid cells spread out. These can be considered part of the middle ear. The middle ear proper contains the three ear ossicles: the malleus, the incus, and the stapes. The foot plate of the stapes is attached to the edge of the oval window by an elastic ligament. The round window is covered by membrane.

Describe the auditory (eustachian) tube.

The eustachian tubes extend from the epipharynx to the middle ear bilaterally. Each has a one-third bony wall, and a two-thirds cartilaginous wall. The pharyngeal opening is slitlike and surrounded by a swelling called the torus. The mouth of the tube is normally closed, but opens intermittently and on swallowing.

Where may the auditory tube be entered, and how may it be found?

It may be entered from the nasopharynx. The *orifice* is at the upper lateral portion of the pharynx, behind the posterior part of the inferior meatus, just above the level of the nasal floor.

Describe the internal ear.

The internal ear is a labyrinth of the three semicircular canals, which are the end organs for equilibration, and the cochlea, which is the end organ of hearing. The vestibule lies between the two. Endolymph and perilymph lie inside the labyrinth. The eighth nerve supplies both the auditory and the equilibratory portion. The internal auditory artery and vein enter the labyrinth with the eighth nerve.

Section 2

PATHOLOGY

RETROGRADE CHANGES AND DISTURBANCES OF METABOLISM

Discuss the retrograde changes that follow injury to tissue.

Among the fundamental results of injury to tissues are the retrograde changes, namely—atrophy, degeneration, and necrosis. Such effects may be caused by a variety of injurious agents, including bacterial and chemical irritants, radiant energy, heat, and nutritional disturbances.

What is meant by fatty metamorphosis? Describe an increase of demonstrable fat in an organ.

This may occur as a large single droplet of fat in a cell, pushing the nucleus to one side (vacuolation), or numerous small droplets throughout the cell, with degenerative changes in its nucleus.

Discuss the factors concerned in fatty metamorphosis.

There are several possible factors concerned in the production of fatty metamorphosis. (1) In the simplest form an excessive amount of fat is brought to a normal cell. (2) The amount of fat brought to the cell may be normal, but the cell, due to some injury (toxins, anoxemia from anemia or impaired circulation), is incapable of utilizing it and the fat accumulates. (3) So-called invisible fat (lipoids) is known to exist in the body cells and when, as the result of disease, the cells disintegrate, this invisible fat becomes visible in the cell body. This process is spoken of as fat phanerosis. Fatty change finally results in liquefaction, caseation, total destruction of cells or necrobiosis.

What is endocrine atrophy?

This atrophy occurs in organs that depend for their functional activity on endocrine stimulation, when such stimulation is decreased or ceases. For example, in Simmonds' disease, cessation of pituitary activity results in atrophic changes in the thyroid, adrenals, ovaries, and other organs that are influenced by pituitary hormones.

Describe amyloid degeneration and state in what cases and in what organs it is found.

Amyloid degeneration is of unknown etiology, commonly occurring as a complication of chronic suppurative disease. Amyloid infiltration affects chiefly the intima of small blood vessels and is characterized by the formation of an albuminoid substance giving a characteristic reaction in the cells and intercellular substance. The most frequent seats are the liver, kidney, and spleen (sago spleen), walls of the intestines, heart, and blood vessels. The cut surface of organs has a waxy or bacony appearance.

Discuss amyloidosis in recurrent polyserositis (familial mediterranean fever, periodic disease).

Recurrent polyserositis is characterized by a peculiar ethnic distribution and the typical features of a recessive autosomal inheritance. The cardinal feature of this disease is a recurrent inflammation of the serous membranes. Symptoms may include fever, abdominal pain, chest pain, joint pain, gastrointestinal disturbances, and headache. The most frequent signs are colloid-body–like dots in the eye grounds, palpable spleen, extreme tenderness, rigidity of abdominal wall, decreased motility of the diaphragm, and pleural and joint effusion. The attacks last from 1 to 4 days and may appear at irregular intervals of 2 days to several months. Amyloidosis is a characteristic and frequent feature of the disorder and is the sole cause of the high mortality. Amyloidosis may precede the appearance of symptoms and is not related to the onset or duration of the disease, or to the number of attacks. It is concluded that the amyloidosis is an independent finding, correlated with, but not caused by, the clinical manifestations.

Discuss injury by ionizing irradiation.

All living cells are damaged by ionizing irradiation, but the degree of susceptibility varies. The most radiosensitive cells are those of lymphoid tissue, blood-forming organs, intestinal epithelium, and germ cells. Less sensitive are the cells of dermal epithelium, vascular endothelium, salivary glands, growing bone and cartilage, the eye, and collagen and elastic tissue. Least radiosensitive are cells of the kidneys, liver, thyroid, pancreas, adrenals, mature bone and cartilage, muscle, and nervous tissue. Effects of irradiation on surviving cells include mutations or permanent alterations in their physiological capabilities. An important delayed or late effect is a tendency of cells injured by irradiation to undergo malignant change. Cancers of skin and of bone have been the most frequent neoplasms produced by localized irradiation, and leukemia has been the most frequent malignancy following whole-body irradiation.

What varieties of degeneration may occur in lymph nodes?

Hyaline and amyloid degeneration; fatty, calcareous, and pigmentary infiltration.

Discuss hyaline degeneration.

Any eosinophilic, structureless, translucent material collecting around cells, usually arising from the surrounding connective tissue, may be called hyalin. It is commonly found in scars, arteriosclerotic plaques, and organs such as liver and kidney. In the kidney and liver hyaline material is seen as droplets.

Necrosis—distinguish between the coagulation and liquefaction forms, with example of each.

Coagulation Necrosis: This is characterized by the production of fibrin, the thrombin being supplied by the broken-down cells. An *example* is the diphtheritic or "false" membrane in diphtheria.

Liquefaction Necrosis: The intercellular substances break down and form fluid or pus, the cells floating in the fluid; no coagulation takes place. This form is often the terminal stage of other forms of necrosis. *Examples are* acute softening of the brain after embolism and the vesicles that follow a burn.

What is cloudy swelling? In what conditions is it commonly found?

Cloudy swelling is one of the most common of all pathological changes in the cells of the liver, kidney, and heart. It consists in imbibition of water by the cells. The cells microscopically appear swollen, cytoplasm granular, and outlines indistinct. Grossly, the organ is slightly swollen, dull, the capsule tight and the tissue pale, and the cut surface bulges.

In hydropic degeneration, the increased water is accumulated in vacuoles, rather than in a diffuse state. Both conditions are reversible and are associated with acute febrile diseases.

Discuss (*a*) caseation; (*b*) calcification.

(*a*) A process similar to coagulation necrosis, which is due to invasion of the tissue by the tubercle bacillus. It affects both cells and intercellular substance, which are converted into a formless mass of granular—so-called "cheesy"—debris, surrounded by nuclei in various stages of degeneration, and an inflammatory zone. The process terminates in liquefaction and absorption, or calcification and encapsulation.

(*b*) The deposition in tissues other than bony tissue of earthy salts, chiefly the carbonates and phosphates of calcium and magnesium. Calcification occurs in tissues with deficient blood supply and is found chiefly in cartilage; the connective tissue of blood vessels (aorta, valves of the heart, especially the aortic); tumors; encysted parasites; necrotic foci; infarcts; thrombi and emboli (phleboliths); ganglion cells of the nervous system; and in the form of biliary, renal, vesical, and intestinal calculi (enteroliths).

THE BLOOD

Describe the pathological changes in pernicious anemia.

The body is not emaciated; the fat is yellow and may be quite abundant. There are hemorrhages in various mucous membranes. The heart is large, flabby, and usually empty. The muscles, including the myocardium ("tiger-lily heart"), are the seat of advanced fatty change. The stomach is atrophied and the liver and spleen enlarged and fatty. Iron is found in excess in the liver, spleen, and kidneys. The bone marrow is red and "lymphoid" and contains gigantoblasts. Foci of sclerosis are present in the cord and also in the brain.

Discuss the pathological picture seen in Hodgkin's disease.

Hodgkin's disease is a disease of the hemopoietic organs—bone marrow, lymph nodes, spleen, and liver. Whether inflammatory or neoplastic is unknown. Microscopically, it is characterized by pleomorphism. The individual lesion is mainly composed of large pale cells of the "epithelioid type," so the picture may resemble the hyperplastic form of tuberculosis. In the lesion there are scattered large multinucleated cells—the *Dorothy Reed, Sternberg,* or *Sternberg-Reed cells.* Various types of white cells are scattered throughout the lesions; characteristically there are numerous eosinophils. Grossly, the disease is characterized by lymphatic enlargement, splenomegaly, and enlarged liver. Organs are infiltrated by suet-like opaque patches. There are fever and generalized cachexia. The disease may run a fulminating course or may be extremely protracted. It is invariably fatal.

Name some of the changes which occur in extravasated blood.

(1) Coagulation, followed by absorption of the fluid elements and deposition of blood pigment, which is also eventually carried off by the lymphatics. The tissue destroyed by the hemorrhage is replaced by connective tissue. (2) Organization—the coagulated blood is replaced by fibrous tissue. (3) Cyst formation—instead of being absorbed, the fluid portion may remain as a cyst. (4) The blood, especially in serous cavities, may become infected and undergo suppuration. (5) Calcification (rare).

What is an embolus? Mention frequent sources of emboli. State the sequels of embolism.

Embolism is the obstruction of a blood vessel by an embolus or fragment of fibrin from a thrombus. Fragments of tissue, tumors, particles of fat, air bubbles, and microorganisms may also act as emboli. The sequels depend on the kind of vessel affected. Embolism of a terminal artery gives rise to an anemic or a hemorrhagic infarct, depending on the organ involved; embolism of a large artery may lead to gangrene of the part supplied; if the blood supply to the motor area of the brain is obstructed, paralysis results; if the embolus is infected, a metastatic abscess develops at the site of lodgment.

What is thrombosis? Describe the manner of its formation.

The coagulation of blood within the blood vessels or heart during life. The causes are some disturbance that impairs the vitality of the endothelium, either in the vessel walls or in the blood, and retardation of the blood stream. The blood platelets or plaques first adhere to the vessel wall and form the nucleus for the clot. Leukocytes are deposited on and around this nucleus, break down, liberate thrombin, and permit the formation of fibrin. Red corpuscles are also entangled in the coagulating mass and give the red color to the thrombus.

Mention the difference between an embolus and a thrombus.

An embolus is a particle of fibrin that separates from a thrombus and lodges in some part of the circulation. A thrombus is a clot that forms within a vessel and is stationary.

Where are emboli most frequently found? Of what do emboli most frequently consist?

In the lungs and brain. Emboli most frequently consist of fibrin clots derived from a thrombus.

Define infarction, and name the organs in which infarction most frequently occurs.

An infarct is a wedge-shaped infiltration of blood within an organ, due to obstruction, usually by an embolus of the artery supplying the area affected. Infarcts are most common in the lung, kidney, brain, and spleen.

INFLAMMATION, REPAIR, AND REGENERATION

Discuss the fundamental phenomena of inflammation.

The most modern concept of the process of acute inflammation is that the initial injury brings about disruption of cells and that the cell contents are released into the intercellular spaces. These substances, directly or indirectly, initiate the process of inflammation. Four of these substances have been identified: (1) *leukotaxine,* the permeability factor, a nitrogen-containing substance originating in injured tissue, is supposed to bring about increased permeability of capillaries, vasodilatation, and stasis of blood after the initial vasoconstriction produced by nervous reflexes from the site of injury; (2) *necrosin,* an injury factor, is a toxic euglobulin that induces damage of tissues and initiates the process of inflammation. It also aids in the formation of fibrin; (3) a *leukocytosis-producing factor,* a pseudoglobulin, that is produced at the site of injury induces leukocytosis by stimulating the bone marrow by way of the blood stream; and (4) *pyrexin,* which is a fever-provoking factor when it enters the circulation. It is a polypeptide associated with the euglobulin fraction of exudates.

Give the types of inflammation.

Classification of inflammation may be according to: (1) duration and severity, as acute, subacute, or chronic; (2)

the predominate nature of exudate, as serous, fibrinous, hemorrhagic, purulent, or catarrhal; and (3) the causative agent, as bacteria, foreign-body reaction, allergy, etc.

What is allergic inflammation?

In allergy or hypersensitivity there is an alteration or heightening of tissue reactivity (hyperergy) to an antigen. The Arthus phenomenon is a marked local allergic inflammation and necrosis, which results when an antigen is injected into the skin of an animal previously sensitized to the same antigenic protein. Disorders produced by hypersensitivity include: (1) the primary diseases of hypersensitivity caused by agents that are not intrinsically harmful—pollens, dusts, foodstuffs, etc., which affect the respiratory tract and nasal sinuses, the skin, and the mucosa of the gastrointestinal tract; and (2) certain nonprotein substances that can induce specific sensitivity by attacking a normal protein of the body, thus producing a new "foreign" protein that stimulates the production of specific antibodies. Such seems to be the mechanism by which sulfonamides, penicillin, and other drugs may produce hypersensitivity reactions. Lesions that can result from hypersensitivity reactions include periarteritis nodosa, pneumonitis, myocarditis, focal necrosis of lymph nodes and spleen, focal collagen degeneration, tuberculoid granulomas, purpura, agranulocytosis, hemolytic anemia, enteritis, arthritis, and glomerulonephritis.

What is the pathology of plastic inflammation?

The exudate contains fibrinogen and the thrombin is supplied by broken-down leukocytes. Fibrin is rapidly formed and causes adhesion between adjacent structures (layers of the pleura or pericardium). The fibrin later becomes organized and permanent adhesions, with obliteration of serous cavities, result.

What is productive inflammation?

In productive or chronic inflammation, the proliferative changes predominate and new connective tissue is formed. Mucous surfaces become thickened, granular (granular pharyngitis), or polypoid (gastric and intestinal mucous membrane). It is also called *interstitial* when occurring in the substance of organs (interstitial nephritis).

Illustrate and define hypostatic inflammation.

Inflammation developing as the result of irritants acting on tissue the seat of hypostatic congestion. Hypostatic pneumonia occurs as a terminal infection in typhoid and other adynamic fevers and always involves the dependent portions of the lungs. Particles of food or secretions are aspirated and act as irritants to the parts already the seat of hypostatic congestion.

Describe termination of inflammation by resolution.

The emigrated plasma and leukocytes re-enter the blood current or are carried off by the lymphatics. The cells, if they are numerous, first undergo softening and are absorbed. The proliferated connective-tissue cells remain in situ or become wandering cells. Phagocytes and enzymes liberated from broken-down leukocytes also take part in the removal of broken-down cells. The tissue returns to its normal condition.

Describe healing by granulation.

✓ The first stage comprises the usual changes incident to inflammation—dilatation of capillaries, exudation of serum, and emigration of leukocytes. The injured connective-tissue cells die and are disposed of by absorption and phagocytosis. On the second or third day small red nodules, called granulations, appear on the wound surfaces. They contain newly formed capillary sprouts, surrounded by proliferated connective-tissue cells. The capillary processes unite with similar processes from an adjacent or the same capillary to form new blood vessels. The newly formed connective-tissue cells or round cells around the capillaries elongate and form new fibrous tissue, which afterward contracts and forms the scar or cicatrix. The epithelial continuity is restored by multiplication of the epithelial cells at the edges of the wound and the healing process is completed.

What is the composition of the inflammatory exudates?

A highly albuminous fluid with a high specific gravity—1.015 to 1.030—and alkaline reaction, containing leukocytes, red blood cells, and a few endothelial (mesothelial) cells.

Discuss the effects of an exudative type of inflammation upon structure, and explain how and why function may be permanently impaired.

In fibrinous pleurisy the two layers of the pleura may become adherent and complete obliteration of the sac result; or the inflammation may terminate in suppuration—*empyema*—with the same result as regards function.

Explain the development of pus corpuscles.

They are leukocytes, chiefly of the polynuclear type, contained in purulent exudates and, as in inflammation generally, are the leukocytes that have passed through the walls of the capillaries.

Define phlegmon, abscess, ulcer, fistula, furuncle, carbuncle, caries.

Phlegmon: diffuse purulent infiltration of a tissue. *Abscess:* a circumscribed collection of pus in the substance of a part or organ. *Ulcer:* localized suppuration on a free surface with tissue destruction. *Fistula:* a suppurating canal connecting a body cavity or hollow organ with another cavity or the free surface of the body. *Furuncle:* a localized suppurative and necrotic inflammation starting in a hair follicle, sebaceous gland, or sweat gland. *Carbuncle:* a more extensive but similar process with multiple lesions and necrosis or gangrene of the skin and subcutaneous tissue. *Caries:* molecular destruction of bone (or teeth) corresponding to ulceration in soft tissues.

Describe the formation of an acute abscess.

Pyogenic microorganisms invade the tissues through a dissolution of continuity in the skin or an organ, by way of the lymph channels, and inaugurate the phenomena of inflammation and suppuration. The collection of pus is localized and separated from the healthy tissue by a line of demarcation called *pyogenic membrane.* This may be the seat of liquefaction necrosis, when the suppuration is spreading, or of regeneration, when the connective-tissue (round) cells are in excess. The abscess continues to spread until it reaches the surface, a process termed "pointing"; rupture then takes place, the pus is evacuated, and the resulting cavity heals by granulation.

Describe the formation of a metastatic abscess.

When an embolus is lodged in a terminal artery, the part supplied by this vessel is deprived of its circulation and becomes anemic; or occasionally a backward flow of blood takes place from the vein into the emptied vessels and a congestion occurs. If the embolus is infected, a metastatic abscess results.

Describe the process of ulceration.

Suppurative inflammation with destruction of tissue, occurring on free surfaces—the skin or mucous membranes. The floor of the ulcer is covered with granulation tissue and pus, and corresponds to the pyogenic membrane of an abscess. Varieties of ulcer are: *phagedenic,* spreading ulcers with rapid destruction of tissue; *serpiginous,* extending in one direction while other parts are healing; *indolent,* dry ulcers with scanty granulations and small tendency to heal; *round* or *peptic* ulcer of the stomach, due to digestion of the wall by the gastric juice; pressure ulcers (*decubitus*) and *perforating ulcer of the foot,* in which the process is necrotic (due to trophic disturbance).

Define regeneration of tissue.

Regeneration is the replacement of destroyed tissue by newly formed similar tissue. Capacity for regeneration decreases as age increases and also is affected by the nutritional state of the individual. The most important factor, however, is the type of tissue destroyed. The more highly specialized the tissue, the less is the capacity for regeneration. Thus, connective tissue regenerates most readily, whereas ganglion cells of the central nervous system have no ability to regenerate. When tissues without the ability to regenerate are destroyed, repair is by connective tissue, or, in the central nervous system, by neuroglial cells. Even in tissues with good regenerative ability, such as the liver, extensive destruction is repaired largely by connective tissue.

Define gangrene.

The putrefaction of dead tissues still attached to the living body.

Briefly describe the types of gangrene, and give the conditions determining each.

Dry Gangrene: The tissues are dark, friable, horny, and mummified and separated from the healthy tissue by a line of demarcation. This form is due to arterial obstruction and evaporation of the tissue juices. It occurs in old age (senile gangrene) from arteriosclerosis; in Raynaud's disease or symmetric gangrene, a nervous affection characterized by spasm of the arteries; and in frost-bite and ergotism, from extreme contraction of the blood vessels.

Moist Gangrene: The affected part is swollen, soft, and pultaceous; the fluids are in excess; the color ranges from dark green to black as the blood pigment breaks down; the surface is covered with blebs and blisters; crepitation can be elicited (gas); the odor is characteristic. In moist gangrene the venous circulation is obstructed; it occurs in severe microbic infections (hospital gangrene); traumatism and severe inflammations destroying the blood vessels or obstructing the veins; diabetes; and nervous (trophic) disturbances (certain bed sores).

LYMPH NODES

What are the usual pathologic findings in infectious mononucleosis? What are the commonest complications?

The lymph nodes and spleen show follicular hyperplasia and abnormal lymphocytes, with thinning of the capsule and trabeculae of the spleen, which may terminate in rupture. The lymphocytic involvement of the liver and hyperplasia of the Kupffer cells explains the jaundice that may occur and the frequent impairment of liver function.

Name the various pathological conditions in which there is enlargement of the lymph nodes.

(1) *Acute lymphadenitis:* usually secondary to pyogenic localized infections, such as a boil. Also seen in certain virus diseases, such as herpes simplex.

(2) *Chronic lymphadenitis:* secondary to a chronic focus of infection.

(3) *Chronic granuloma:* tuberculosis and syphilis (Hodgkin's disease and Boeck's sarcoid are often classified in this group).

(4) *Lymphoblastoma or malignant lymphoma:* including Hodgkin's disease, leukemias, and lymphosarcoma.

(5) *Generalized lymphadenopathy:* characteristic of infectious mononucleosis. It is also commonly associated with acute febrile illness in children and adolescents.

BONES AND JOINTS

Give a minute description of and explain the process occurring in necrosis of bone.

Necrosis is death of a large or small portion of bone in mass and is due to interruption of the blood supply. This may occur in periosteitis, osteitis or osteomyelitis, or embolism. The dead fragment, called a *sequestrum,* is irregular in outline and more or less eroded. It becomes separated from the healthy bone by a process of demarcation, as in necrosis of soft parts. The sequestrum, like any foreign body, causes *suppuration* of the surrounding tissues. *Fistulas* are usually present. A peripheral sequestrum may be discharged, and the loss may be made good by proliferation of the periosteal cells. If the sequestrum is central, discharge is impossible, and the sequestrum becomes surrounded by hyperplastic material, causing thickening of the bone.

What pathologic changes occur in caries?

Caseous degeneration and formation of *granulation tissue,* followed by softening and the production of a semifluid, cheesy material containing particles of bone. An abscess with a pyogenic membrane covering the walls of the cavity may result. The carious focus or abscess may become encapsulated by the formation of granulation tissue and cicatrization or new formation of bone.

Give the pathology of spina bifida.

The posterior processes of the vertebrae fail to close and the membranes of the spinal cord protrude through the cleft in the form of a hernial sac. The hernia may be covered with skin or only with pia.

Describe the reparative process following the fracture of a long bone.

The successive phases are hemorrhagic extravasation in the marrow and at the line of fracture; congestion and cellular infiltration of the periosteum, marrow, and bone; formation of new blood vessels and proliferation of cells; deposition of calcium and formation of bone and cartilage. The newly formed bone is called *callus;* the outer portion is derived from the periosteum and is called the *periosteal* or *ring callus,* and the central portion (*pin callus* or *myelogenous callus*) is derived *from the marrow.* After absorption of the excessive callus is completed, some thickening persists at the site of fracture.

What changes characterize inflammation of bone?

(*1*) *Suppurative Inflammation:* Softening of the bone by absorption of the calcium salts and formation of granulation tissue by proliferation of the cells in the marrow and in the haversian canals (*rarefying osteitis*). Localized abscesses or purulent infiltration with necrosis results.

(*2*) *Hypertrophic Inflammation:* Deposition of bony tissue, as in normal bone formation, and increase in the density of the bone (*condensing osteitis*).

(*3*) *Degenerative Inflammation:* Absorption of the calcium salts and increased porosity of the bone (*inflammatory osteoporosis*); formation of cavities containing bone corpuscles (*osteoblasts*) and giant cells—so-called "Howship's lacunae"; increased vascularity and perforation by newly formed blood vessels, establishing communications between neighboring lacunae.

Describe briefly the pathology of arthritis deformans.

Two forms of the disease are distinguished:

(*1*) *Proliferative Form* (*Progressive Polyarthritis*): Many joints are involved, become swollen and painful, but remain soft. Later the articular cartilage is partly absorbed and in part replaced by osseous tissue; the ends of the bones become rarefied, as shown by the x-rays, but there is no formation of bony nodules (exostoses) about the joint cavity. There may be loss of calcium salts, and the synovial membrane becomes thickened. Granulations form on the synovial membrane and on the cartilage covering the articular surfaces, and, with similar granulations on the opposing surface, form adhesions that partially obliterate the joint cavity (arthritis adhaesiva). The bone marrow takes part in the process and becomes converted into a fibrous tissue containing many capillaries and osteoblasts, which invade the cartilage so that it is replaced by bone. In the end, fibrous or bony *ankylosis* results. The ligaments in the spine may become ossified, resulting in a rigid spinal column.

(*2*) *Degenerative Form* (*Osteoarthritis Deformans*): In this form the enlargement of the joints is due to the formation of hard nodules in and about the margin of the joint. The hands and feet are chiefly affected, the former showing a characteristic deformity: flexion of the fingers with deflection to the ulnar side; nodular enlargement of the knuckles and of the terminal phalanges. The backs of the hands appear hollowed out; the skin is paper-like, shiny, and translucent. There are no granulations in the joint cavity. The cartilage first becomes fibrillated and shaggy, then eroded, and finally ulcerated, exposing the ends of the bones, which are smooth and hard. Cartilaginous or bony outgrowths surround the enlarged joint cavity and interfere with movement, but there is no true ankylosis (Heberden's nodes).

Describe the structural changes that occur in tuberculous joints.

The synovial membrane becomes thickened and edematous and sometimes ulcerates; the joint cavity becomes filled with a serous exudate; tubercles develop in the joint and synovial membranes; and the synovial membrane now becomes shiny, smooth, and nodular. Fringes of the synovial membrane spread over the borders of the articular cartilage and become adherent to it; the cartilage becomes eroded and destroyed, and pieces of it become detached, leaving the bone denuded. The bone now is attacked by the tuberculous process. There may be adhesions, subluxation, erosion of the socket, or other joint deformity.

Describe the pathologic conditions produced by Pott's disease.

The affected vertebrae are replaced by granulation tissue and the intervertebral disks are absorbed. In favorable cases the tuberculous process is arrested at this stage, fibrous tissue replaces the granulations, and ankylosis with little deformity or functional disability results. In severe cases the process of caseation goes on until the vertebrae are completely destroyed or converted into a sequestrum lying in a caseous abscess. The pus later finds its way toward the surface and a spinal abscess results. Finally, the vertebrae above and below the seat of the disease approach one another, and a prominence, known as an "angular curvature" (kyphosis) is formed. This deformity is permanent and is associated usually with a compensatory lordosis in the lumbodorsal region.

TUMORS

List the chief advances of experimental cancer research.

(1) That certain tumors are transplantable from animal to animal within a given species. (2) That malignant tumors can be initiated by the use of chemical "carcinogenic" agents. (3) That certain tumors can be transferred by means of a cell-free filtrate or extract and are apparently of viral origin.

What is understood by the phrase "new formation"?

The apparently causeless formation in some portion of the body of a mass of tissue that does not serve any useful purpose.

Mention the general characteristics of a benign tumor, as distinguished from a malignant tumor.

Benign tumors, in contradistinction to malignant tumors, are usually encapsulated, grow slowly, do not infiltrate, do not metastasize, do not recur after removal, produce no cachexia, and are composed of well-differentiated mature cells.

Define sarcoma and carcinoma and give the usual method of metastatic extension of each.

Sarcoma: a tumor in which the cells predominate so that the intercellular substance is quite insignificant.

Carcinoma: a histologically atypical tumor, composed of epithelial proliferations and a well-developed connective-tissue stroma.

Metastasis: takes place through the blood vessels in sarcoma. Carcinoma extends by: (1) infiltration of the surrounding tissue; (2) by metastasis along the lymphatics, and sometimes (3) through the blood vessels (portal circulation).

(a) On what principle are tumors classified? (b) Mention the important classes of tumors, giving an example under each class.

(*a*) According to the type of tissue from which they are derived, and according to their *benign* or *malignant* character.

(*b*) (1) Connective-tissue tumors: benign, fibroma; malignant, fibrosarcoma. (2) Muscle-tissue tumors: benign, leiomyoma; malignant, leiomyosarcoma. (3) Epithelial-tissue tumors: benign, adenoma; malignant, adenocarcinoma. (4) Elements of the nervous system: benign, neuroma; malignant, neuroendothelioma. (5) Endothelial tumors: endothelioma. (6) Tumors of complex tissues: simple mixed tumors, teratomas, embryomas.

(a) Define and illustrate the term physiologic prototype as applied to tumors. (b) As a rule, what are the respective ages of occurrence of carcinoma and sarcoma?

(*a*) The physiologic prototype of a tumor is the type of normal cell to which the cells of the tumor conform. Example: A sarcoma is a connective-tissue tumor, i.e., a tumor the cells of which are connective-tissue cells. (*b*) Carcinoma occurs in middle and advanced life (more than 40 years of age), sarcoma in children and young adults (up to 40 years).

The etiology of tumors: (a) What influence has age especially as to the connective-tissue type? (b) Sex, if a significant factor, denotes a predisposition to what? (c) What is the significance of heredity? (d) Of local causes?

(*a*) Connective-tissue tumors are most common in *early life,* when the connective tissues grow most vigorously. (*b*) *Sex* has little bearing on the etiology of tumors, except in the case of cancer of the genital organs (including breast) which is more common in females. (*c*) *Heredity* is considered by some to be an etiological factor; but the more probable view is that the predisposition to tumors and the weakened resistance of the tissues are hereditary. (*d*) As to *local predisposing factors*—irritation is held to be an exciting cause (cancer of the lip in smokers; cancer of the cervix developing in an old laceration; cancer developing in gastric ulcer).

What are the commoner intrathoracic tumors? Describe them briefly and their relationship to surrounding organs.

Metastatic lesions of lymph nodes or lung; primary tumors of bronchi, lungs, trachea; carcinoma of esophagus; tumors of lymphoid tissue (lymphosarcoma, Hodgkin's granuloma). Metastases may occur from almost any primary site in the body, either to mediastinal lymph nodes, causing compression of local structures, or to lung parenchyma.

Primary carcinomas of the lung arise in a large majority of cases in the bronchi, eparterial or suparterial more commonly, and are usually epidermoid in character. Adenocarcinomas, less frequent, occur in the second or third bronchial branches, toward the periphery of the lung. Some tumors are characterized by the morphology of the cell (oat cell) or are undifferentiated. Tumors may cause thickening and ulceration of the bronchial mucous membrane with stenosis. If the bronchus is occluded from stenosis or a sessile or polypoid growth, the parenchyma behind the obstruction usually develops an organizing pneumonia, often with abscess formation. Males are much more commonly affected. Adenomas or polyps are common in the larger bronchi. The rarer alveolar carcinoma, arising in the lung parenchyma in the periphery, in contrast to the bronchi, may have multiple regional sites of origin. Uncommon mesotheliomas involve the parietal rather than the visceral pleura in a marked thickening of dense connective tissue with polygonal and round cells. The uncommon superior pulmonary sulcus tumor (Pancoast tumor) arises at the apex of the lung and may be epidermoid in character, adenocarcinoma, or of sympathetic nervous-tissue origin. From pressure or involvement of adjacent sympathetic ganglia, Horner's syndrome may develop (homeolateral ptosis, myosis, enophthalmos, anhydrosis, and flashing) and brachial paresis or paraesthesia of the hand.

Carcinoma of the esophagus, commoner in men than women, occurs in the middle third, or lower portion (but also at the pharyngeal esophageal junction). It usually ulcerates and invades and is adherent to the surrounding structures, leading to deglutition, infection locally or in the lung from overflow.

Lymphoid tumors may arise in the mediastinal lymph nodes or they may participate in a systemic involvement. The pathological picture resembles the characteristics of the type elsewhere (Hodgkin's disease; lymphosarcoma; granuloma, tuberculous or nonspecific) and pressure symptoms are produced. Substernal thyroid and thoracic aneurysms, by pressure and space-taking properties, cause symptoms referable to the organs involved.

Describe the appearance, types, and locations of the commonest malignant tumors of the gastrointestinal tract.

Stomach: In the United States, second only to the colon in frequency in the gastrointestinal tract and more frequent in males than in females. Along the lesser curvature in the prepyloric region, less common toward fundus, or along greater curvature. May be ulcerative in type or fungating; the latter is more "silent" and projects into the lumen as a large soft mass, which may show superficial ulceration. The ulcerative type is more frequent, varying in size, but usually larger than a benign ulcer, roughly circular with elevated rolled edges and irregular crater, extending into the muscularis with thickening of the mucosal coat, which may be contracted and streaked and exhibit frequent adhesions.

Colon: Now the most common malignant tumor of the gastrointestinal tract and as common in females as in males. About one half occur in the rectum, one quarter in the sigmoid, and the remainder in the colon itself, most frequently in the hepatic flexure and descending portion. Most common types are (1) adenocarcinoma, as ulcerated, nodular lesions with elevated indurated edges, penetrating into the muscularis and peritoneal coat, with adherence to or invasion of surrounding tissues and organs; (2) scirrhous, tending to constrict the lumen; (3) large, fungating carcinomas, mucinous in character, commonest in cecum; or (4) papillary type, usually multiple with minimal invasion of the wall. Polyps are associated quite frequently with carcinoma and a small percentage show malignant characteristics. Carcinomas also develop in a small number of cases of chronic ulcerative colitis.

Liver: About 10 per cent of gastrointestinal-tract carcinomas occur in the liver and biliary passages. Very frequently arise in cirrhotic livers, less frequently in hemochromatosis. Liver-cell carcinoma (hepatoma) much commoner than bile-duct carcinomas and commoner in males. There are numerous large and small soft nodules, umbilicated and projecting above the surface, grayish red, frequently hemorrhagic, and partially necrotic. Bile-duct carcinomas are usually firmer, more dense, and whiter.

Gallbladder: Most frequently associated with gallstones. May be an infiltrating and ulcerative adenocarcinoma in the gallbladder wall, invading the liver, or papillary with less thickening of wall and little invasion of wall and the adjacent liver. Less frequently, it may be mucinous and more bulky, tending to fill the gallbladder.

Pancreas: More commonly located in the head of the pancreas, usually firm and dense, an adenocarcinoma arising from the ducts or acini.

What are carcinoid tumors?

Carcinoid tumors (argentaffinomas) are distinctive neoplasms that have infiltrative and metastasizing potentialities but are of a low grade of malignancy. The tumor cells are believed to arise from Kulchitsky cells, argentaffin and chromaffin cells found at the base of Lieberkühn's glands, which produce serotonin (enteramine, 5-hydroxytryptamine). Approximately 60 per cent of carcinoid tumors occur in the appendix and the others arise from the remainder of the gastrointestinal tract, any part of which may be involved, although the ileum is the most frequent site. A small proportion may have liver metastases which produce excess serotonin and a distinctive clinical syndrome (carcinoid) that is characterized by episodic flushing of the skin, a plethoric coloration, diarrhea, asthma-like breathing, and cardiac symptoms. In the late stages there may be marked wasting, weight loss, and cutaneous telangiectases or pellagra-like lesions. The large amount of serotonin produced by a functioning carcinoid tumor results in an excess of 5-hydroxy-3-indoleacetic acid in the urine, a valuable laboratory diagnostic test.

How does sarcoma differ histologically from carcinoma?

Sarcoma is made up of embryonal connective-tissue cells with little intercellular substance; the blood vessels are also embryonal and imperfectly formed, without distinct walls. *Carcinoma* is composed of epithelial cells arranged in plugs or acini, without intercellular substances, surrounded by a connective-tissue stroma containing well-developed blood vessels.

Define fibromata. Give the histology of fibromata.

A benign tumor of slow growth consisting of fibrous tissue. The fibrous tissue is poor in cells and consists chiefly of a dense intercellular substance with few blood vessels.

Describe in detail the pathology of uterine fibroids.

Rounded, circumscribed tumors consisting of smooth-muscle fibers and fibrous tissue, arranged in bundles or layers. They are hard, and on section present concentric or irregular lamellae. Calcification and cystic change, due to softening or to distention of the lymphatics, often take place. According to their relation to the uterus three varieties are described: (1) *submucous;* (2) *interstitial* or mural; and (3) *subperitoneal.* The first and third varieties may be pedunculated.

Fibroids are pathologically benign, but practically require operation on account of the pressure they exert, their interference with labor, and the metrorrhagia and endometritis to which they give rise. Submucous fibroids are sometimes expelled spontaneously from the uterus, and subperitoneal tumors may become free bodies in the abdominal cavity.

What determines the benign or malignant nature of a new growth?

BENIGN

Do not disturb the general health.
Have no tendency to recurrence.
Have no metastasis.
Remain within the tissue in which they originate.

MALIGNANT

Profoundly affect the general health.
Recur after removal.
Give rise to metastasis.
Break through the limits of the parent tissue and invade the surrounding structures.

Define (*a*) neuroma; (*b*) angioma.

(*a*) *True neuroma* is a tumor composed of nerve fibers, either medullated (myelinic neuroma) or nonmedullated (amyelinic neuroma). *False neuroma* is a fibrous growth originating in nerve sheaths.

(*b*) A tumor-like formation composed principally of blood vessels.

Describe the pathologic histology of epithelioma and carcinoma.

Squamous-cell carcinoma (epithelioma) arises from the outer cellular layer of the epidermis, is characterized by invasion of the corium with masses of cells reproducing the keratinized portions of the epidermis, with a central area of fully keratinized cells surrounded by polygonal squamous cells (epithelial scar). Basal-cell epithelioma (rodent ulcer) arises from the lower layers of the epidermis or hair follicles; cells are more cuboidal and show no tendency to keratinization. Both usually ulcerate, but ulceration is more destructive in the latter.

Carcinoma (either cylindric-cell or glandular-cell cancer may be meant): In cylindric-cell cancer or epithelioma, columnar cells or goblet cells are found near the periphery of the cancer nests; in the glandular-cell form the cells are polyhedral.

(*a*) Mention two benign breast tumors. (*b*) What are the gross physical findings which may help differentiate benign and malignant breast tumors?

(*a*) *Fibroadenoma; papillary cystadenoma.*

(*b*) Benign tumors are circumscribed, freely movable, smooth, and unattached to either the skin or underlying fascia. In the early stages a carcinoma may feel exactly like a benign tumor. Hence, *any* suspicious mass in the breast should be biopsied, and frozen sections should be made. It is only after local lymphatic spread has occurred that carcinoma can be easily differentiated by physical examination.

Describe the macroscopic and the microscopic appearance of carcinoma of the breast.

In the later stage the skin is thickened, adherent, and stippled, the nipple is retracted, the gland feels hard in places. The axillary nodes are enlarged. If the process is allowed to go on, ulceration develops.

The varieties are the medullary, simple, and scirrhous. *Medullary* or *soft* cancer consists almost entirely of epithelial cells and contains an abundance of "cancer juice"; in the *scirrhous* form bundles of connective tissue inclosing collections of cancer cells are the prominent features; *simple* carcinoma occupies an intermediate position as regards the proportion of epithelial cells and fibrous tissue.

Give the gross and the microscopic appearance of an epithelioma of the lip.

An irregular, nodular elevation with ulcerated surface and infiltrated base. The microscopic appearance is that of squamous cancer.

What pathologic changes may cicatrices undergo?

Carcinomatous, keloidal, ulcerative, and abscess formation.

What are cysts? How are cysts formed? Give the varieties of cysts.

The varieties of cysts are:

(*1*) *Nontumorous:* (*a*) Extravasation cysts, resulting from hemorrhage, followed by absorption of the blood pigment and encapsulation. (*b*) Softening cysts, from circulatory disturbance, liquefaction necrosis, and encapsulation. (*c*) Parasitic cysts, as echinococcus or hydatid cyst.

(*2*) *Neoplastic Cysts:* (*a*) Retention cysts, resulting from obstruction and distention of gland ducts (follicular, mucoid, congenital) followed by distention and accumulation of the secretion. The epithelium lining the cyst is the same as that of the gland. (*b*) Dermoid or teratoid cysts. These develop from misplaced embryonal rests. (*c*) Proliferation cysts or cystadenomas, formed by the proliferation of the epithelial cells of gland acini and secretion of the cells. They are usually multiple.

Give pathology of cystic ovary.

Simple follicular cysts result from distention of the graafian follicles. The cavities are lined with epithelium and the contents are serous or blood-tinged. The cyst may be unilocular or multilocular. The organ is considerably enlarged.

What are teratomata?

Tumors containing elements of different tissues in a situation where they do not occur normally. They result from misplacements or inclusions of tissue during embryonal life, are mostly cystic (dermoid cyst), and contain various *epidermal structures,* such as hair, teeth, sweat glands, and the like.

Is there an association between acute dermatomyositis and neoplastic disease?

In some series, carcinomas, sarcomas, and lymphomas have been found in association with dermatomyositis in over 50 per cent of adult cases. The commonest associated malignancy in women is carcinoma of the breast and, in men, bronchogenic carcinoma.

INFECTIONS

What is the pathology of erysipelas?

✓ A severe inflammation of the skin and subcutaneous tissues due to infection by group A hemolytic streptococci, accompanied by the formation of blebs, and usually ending in resolution, but sometimes in general septicemia and death.

In complicated cases, inflammatory edema and sometimes suppuration are found postmortem. The cocci are found in the lymph spaces. Infarcts occur in the lungs, spleen, and kidneys; malignant endocarditis and septic pericarditis and pleuritis may develop in erysipelas. The meninges are rarely involved. The kidneys show acute nephritis.

What are the characteristic features of diphtheritic exudation or infiltration of mucous ✓ membrane?

The formation of a grayish membrane of varying thickness, firmly adherent, and sometimes extending deeply into the tissues; early failure of the nuclei to take the stain; the deposition of granular or fibrillar fibrin, or, in the form of a homogeneous mass, in the cells and intercellular substance. The process is a *coagulation necrosis.*

Mention some pathologic lesions that are sometimes the sequelae of diphtheria.

Myocardial degeneration, nephritis, necrotic foci in the liver, degeneration of the peripheral nerves.

Describe the major pathologic lesions found in acute rheumatic fever. What are the commonest residua? What effect may these have on general body functions?

Joints: Edema and congestion of the periarticular tissue, increase in synovial fluid, hyperplasia of synovial cells and focal accumulation of mononuclear cells (Aschoff bodies).

Heart: Pancarditis, fibrinous pericarditis; myocarditis with Aschoff bodies, mainly in the perivascular tissue in ventricle and auricle. Valves—small verrucae on the line of closure of the valve, with thickening of the valve on healing, producing incompetence or stenosis. Inflammation and cellular infiltration, resembling Aschoff bodies, in the walls of the large vessels and similar cellular collections in the lungs and subcutaneous tissue. Healing may be complete with but slight residua or recurrent attacks may result in rigid valves and this lead to marked hypertrophy of the heart and incompetence or stenosis of the mitral or aortic valve, most commonly complicated by frequent attacks of decompensation, leading to chronic generalized passive congestion of lungs, liver, kidney, and other visceral organs, with impairment of their functions.

Describe the most characteristic anatomic lesion of typhoid fever.

The *typhoid ulcer* is the end-stage of hyperplasia and necrosis of a Peyer's patch. The swelling is due to the accumulation of round cells, which compresses the vessels and causes necrosis of the lymphoid elements. The ulcer has the shape of a Peyer's patch; its axis is usually longitudinal.

What structures are principally involved in bubonic plague? How are these structures affected?

The lymph nodes, lungs, skin, and mucous membranes, kidneys, spleen, and gastrointestinal tract.

The *inguinal nodes* are most often affected, then in order, the axillary, cervical, and popliteal; enlargement ending in resolution or suppuration. Rarely gangrene occurs. The *lungs* may be the seat of a bronchopneumonia or a primary plague pneumonia. Petechiae and carbuncles develop on the skin ("plague spots"), and hemorrhages from mucous membranes occur. The kidney lesion is an acute general nephritis; the spleen is enlarged (hyperplastic splenitis); the intestines are the seat of hemorrhagic gastroenteritis.

Give the process of tubercle development.

Invasion of the tissue by tubercle bacilli is followed first by an inwandering of polymorphonuclear leukocytes. These soon disappear or are obscured by the development of the *epithelioid cells,* the characteristic feature of the tubercle, and of the multinucleated *giant cells,* which are found chiefly in the central portion. Epithelioid and giant cells are derived from wandering macrophages. In the marginal portion of the tubercle round, mononuclear lymphoid cells collect ("round-cell inflammation"). The tubercle now appears as a gray, translucent body (*gray tubercle*). The tubercle bacilli are found within the giant cells or in or between the epithelioid cells. The tubercle is devoid of blood supply. Further changes consist in hyaline degeneration and fatty infiltration, coagulation necrosis and caseation, resulting in the production of the *yellow tubercle.* Ultimately encapsulation and calcification may also occur, and such nodules and scars remain as evidences of healing.

What is a giant cell? Give characteristics.

A large cell containing several nuclei, formed either by the fusing of several cells or by division of nuclei and increase in the cytoplasm, without further division of the body. They are mononuclear cells generally. The nuclei may be three or four in number, or a score or more. In the Langhans giant cell of tuberculosis, they are usually at the periphery, while in the foreign-body cell they are more central or diffuse. Giant cells occur in granulation tissue, bone marrow, tubercles, gummas, and in giant-cell sarcomas.

Describe the pathology of acute miliary tuberculosis.

A general infection of the body by way of the blood channels, the source of infection in most cases being a pre-existing tuberculous focus in the lungs, lymph nodes, bones, or kidneys. The tubercles are small, of the gray miliary type, and scattered throughout the body, upon the pleura and peritoneum, in the lungs, liver, kidneys, lymph nodes, and spleen; on the meninges, in the bone marrow, and sometimes in the choroid coat of the eye.

Describe the lesion in infectious hepatitis.

Early in an acute case, degeneration of the hepatic cells, with disturbance of architecture leading to necrosis in the central zone and loss of cells; in more advanced cases with infiltrations of periportal spaces with monocytes and leukocytes. In fulminating cases, the liver is small, soft, and a mottled yellow-red, with diffuse granular necrotic debris of liver cells and more intense cellular infiltration, including plasmocytes, lymphocytes, and eosinophils. Spleen and regional lymph nodes are usually enlarged and congested and may be edematous. Bone marrow may be hyperplastic and hemorrhages may occur in many tissues and organs. Recovery may be complete with restoration of normal architecture or, in subacute cases, may result in lobular type of cirrhosis.

Describe (a) the syphilitic lesions of the skin. (b) The lesions in lupus vulgaris.

(*a*) *Syphilis:* The *primary lesion* of syphilis is the *chancre.* An indurated raised, circumscribed, indolent ulcer usually located on or about the genitalia, but one that may be found anywhere on the skin or mucous membranes. There is an associated satellite lymphadenopathy. The *secondary syphilids* are symmetric and polymorphous, run a definite course, involve the superficial parts of the skin, and leave little, if any, scar. The lesions are erythematous, papular, and pustular. The *macular* syphilid, or syphilitic roseola, is circular, of a faint rose-red color, later changed to purple and yellowish red, and but little raised above the skin; it disappears on pressure. The *papular* syphilid consists of firm, fleshy red elevations from the size of a pinhead to 1 inch in diameter. Lenticular and miliary papular syphilids are described, according to the size of the lesions, the miliary being very rare. The *pustular* syphilid may develop primarily or from a macular or papular eruption. The lenticular (varioliform) and miliary (acneform) are differentiated. The former are small, hemispheric, pea-sized pustules with a hard base surrounded by an inflammatory areola. The miliary pustules range in size from a millet seed to a pinhead and occur in groups. Both varieties are covered with crusts.

(*b*) *Lupus Vulgaris:* This appears in the form of irregular patches of reddish, variously sized nodules or tubercles which spread peripherally and ultimately undergo coagulation necrosis and ulceration, leaving after healing smooth white scars. The lupus nodule consists of small round cells at the periphery, a zone of larger epithelioid cells, and in the center of the lesion giant cells containing many nuclei. Tubercle bacilli in small numbers are found in the lesions.

Describe a syphilitic gumma.

A round tumor, ranging in size from that of a pea to that of a small apple, raised above the surrounding surface, and of variable consistency, with a tendency to central softening. The center contains grayish or yellowish "gummy" material, due to mucoid degeneration. The connective tissue is abundant and forms a capsule and radiating trabeculae within the gumma. Microscopically, epithelioid, round, and giant cells are seen, with thickening of the intima of the blood vessels. Gummas on surfaces tend to ulcerate; within organs they usually undergo absorption.

HEART AND BLOOD VESSELS

What pathologic lesions are present in pericarditis?

Four varieties of pericarditis are recognized:

(*a*) *Serous:* The sac is filled with

serum containing flakes of fibrin, some of which adhere to the pericardium.

(*b*) *Fibrinous:* Abundance of fibrin with little serum occurs; adhesions between the two layers are common. The fibrin is disposed in ridges or small, villous projections (*cor villosum*).

(*c*) *Serofibrinous:* This is a combination of the two preceding forms.

(*d*) *Purulent:* The pericardium is covered with pus and fibrin and the cavity contains a thick, purulent exudate.

Name the conditions that give rise to hypertrophy of the heart and explain how they act in so doing.

(*1*) *Mechanical Pressure from Without:* Tumors or adherent pericardium. The hypertrophy is soon followed by atrophy.

(*2*) *Valvular Lesions:* The hypertrophy is a compensatory process, the object being to overcome the increased resistance. Different chambers of the heart are affected according to the seat and character of the valve lesion. It is greatest in aortic regurgitation and stenosis and chiefly involves the left ventricle.

(*3*) *Hypertension, Arteriosclerosis, Aneurysm, Chronic Nephritis:* The resistance to the propulsion of the blood is in the arterial system.

(*4*) *Circulatory Disturbances in the Lungs:* These may be due to congenital heart diseases, emphysema, fibroid phthisis, or other disease of the lungs.

What changes take place in hypertrophy of the heart?

The cavity is enlarged and the wall increased in thickness. Rarely the size of the cavity is unchanged (simple or pure hypertrophy) or even diminished (concentric hypertrophy). The ventricles are chiefly affected.

Give the etiology and pathologic nature of acute endocarditis. If the patient recovers, what permanent pathologic condition results?

Etiology: Acute infections, chiefly rheumatic, also scarlet fever, pneumonia, syphilis (aortic disease). Streptococci, staphylococci, and pneumococci are the most common bacteria concerned.

Pathologic Anatomy: First, a line of roughness forms across the valve near the free edge; small nodular elevations, like beads, or distinct wart-like elevations make their appearance (*verrucose* or *simple endocarditis*); or ulcers may form (*ulcerative* or *malignant endocarditis*).

Results: Simple endocarditis heals by absorption of the fibrinous deposits on the valves and cicatrization, which produces more or less deformity, so that the valves fail to perform their function and chronic endocarditis results (valvular disease with regurgitation or stenosis).

What is subacute bacterial endocarditis? How does it differ from the ordinary acute form?

The disease was practically always fatal after a more or less protracted course until the introduction of massive penicillin therapy, which has lowered the mortality to 20 to 30 per cent. It develops usually on a damaged valve, either acquired or congenital, in contrast to acute endocarditis, which often attacks normal heart valves. The bacteria most commonly involved are the *Streptococcus viridans;* next in frequency are the enterococci. The mitral and aortic valves are chiefly affected. The lesion, or "vegetation," consists of an inflammatory exudate containing fibrin, red and white blood cells and platelets, necrotic endothelial cells, and the causative bacteria in abundance. The spleen is enlarged and there is embolic focal nephritis.

Describe how aortic regurgitation affects the cavities and musculature of the heart.

In *aortic regurgitation* the left ventricle is chiefly affected, becoming greatly hypertrophied—so-called *cor bovinum.* Enlargement of the right heart occurs late.

Describe the appearance of the heart in an advanced case of mitral stenosis. What are the effects of mitral stenosis on other organs? Explain how these effects are brought about.

The left atrium is greatly enlarged (hypertrophy and dilatation) because of the great increase of intra-atrial pressure toward the end of atrial diastole, as the blood, returning from the lungs, finds an insufficiently emptied atrium. Owing to the increased intrapulmonary pressure the right ventricle, as in mitral insufficiency, also undergoes dilatation and hypertrophy. The left ventricle is not, as a rule, enlarged unless mitral insufficiency is also present; it may even be reduced in size. The leaflets of the mitral valve are thickened and the edges may be partly adherent to one another; or the narrowing may be due to constriction of the ring and calcareous deposits projecting into the orifice. When compensation fails, relative tricuspid insufficiency and congestion of the systemic veins, the liver and spleen ultimately supervene.

State the results of stenosis of the tricuspid valves of the heart.

Dilatation of right atrium, cyanosis of the face, jugular pulsation, passive hyperemia of pulmonary and abdominal organs, pulsation of liver, general anasarca.

Describe the spleen and kidneys from an individual dead after a long-standing mitral insufficiency.

The organs present the condition known as *cyanotic induration,* consisting in hyperplasia of the connective tissue, contraction and atrophy of the parenchyma, with pigmentation. The organs are small and intensely hard.

Explain why and how obstructive disease of the coronary arteries causes myocardial degeneration.

The terminal branches of the coronary arteries are *end-arteries,* that is, the only communication between them is through capillaries. If one of the vessels is blocked by a thrombus or an embolus, a *white infarct* (an area of anemic necrosis) results. Such areas of necrosis may become gradually transformed into scar tissue and thus lead to the production of fibrous myocarditis; more often the myocarditis is caused by an obliterative endarteritis of some of the coronary branches, which interferes with the nutrition of the heart muscle.

What are the degenerative changes of arteries?

Fatty, hyaline, calcareous, and amyloid.

Describe the pathologic conditions present in atheroma.

Atheroma is a stage in the process of arteriosclerosis characterized by fatty infiltration of the intima and media.

Describe the sequence of events in congestive heart failure and the resultant changes in the organs.

Regardless of the primary cause, the probable sequence of events seems to be inadequate cardiac output; decreased renal function with retention of salt and water, which leads to increased blood volume, edema, and increased venous pressure and, because of the inability of the myocardium to maintain adequate cardiac output, further stagnation; and increased venous pressure, with continuation in a vicious circle. After an almost imperceptible peripheral edema, dilatation of the heart begins, first on the right side, concomitant with a slowing of the venous return from the visceral organs; then congestion of lungs, then liver, kidney, etc.; dilatation of the left side of the heart, with an aggravation of the conditions throughout the entire system. *Lungs* become deep red and larger and firmer than normal, decreasing pulmonary capacity and rate of blood flow. Their increase in size and decreased respiratory expansion raise the intrathoracic pressure, further impeding the return of blood from the periphery. Continued congestion leads to fibrosis and deposition of hemosiderin in macrophages in the alveolar walls and vesicles. *Liver* becomes enlarged and firm, with venous congestion; it has a smooth, tense capsule. Pressure atrophy results from the dilated sinusoids, particularly in the central portion of the lobule, brownish yellow in color, surrounded by the deeply congested parenchyma in the portal zones. Coalescence of these areas suggests the appearance of a nutmeg. *Spleen* becomes enlarged, firm, and deep purplish, with a thickened capsule and prominent trabeculae with indistinct malpighian bodies. Hemosiderin is evident on microscopic examination. *Kidneys* are slightly enlarged, firm, and deep red, oozing large quantities of blood on section. The pyramids are deep purple, contrasted with the paler red striated cortex. All capillaries are dilated and filled with blood, and the tubular epithelium may be degenerated. *Gastrointestinal tract* is heavy, thick-walled, and waterlogged, particularly in the mucosa.

Discuss the so-called collagen diseases. Describe a common visceral lesion.

Polyarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, acute rheumatic fever, and rheumatoid arthritis. All are characterized by widespread involvement of blood vessels, smooth muscle, and connective tissue, and all seem related to some type of prolonged anaphylactic reaction.

The basic underlying lesions consist mainly of fibrinoid changes in collagen and in the ground substance, necrosis and inflammation of arteries, formation and collection of cells resembling Aschoff bodies, and distinctive pneumonitis. Characteristic lesions are necrotizing and inflammatory changes in the arteries (polyarteritis nodosa), hyaline thickening of the glomerular capillaries ("wire loop" lesion of disseminated lupus), atypical varicose endocarditis of Libman-Sacks type (lupus erythematosus), Aschoff bodies (acute rheumatic fever).

Describe the autopsy findings, as regards the vascular and urinary systems, one would expect in a case of arteriosclerosis of long standing.

The intima of the arteries becomes thickened and at first translucent (*hyaline degeneration*); later firm, opaque, and yellowish white (*atheroma*); and finally hard from infiltration with lime (*calcification*). The atheromatous patches may break down (liquefaction necrosis), leaving ulcers (*atheromatous ulcers*). The media and adventitia become more robust by the production of fibrous connective tissue, compensating in a measure for the loss of elasticity. Arteriosclerosis may be circumscribed (nodular) or diffuse. The various processes are usually seen at the same time in different portions of the vascular system. The veins are sometimes involved, especially in the portal system (phlebosclerosis or angiosclerosis). The *heart* is often greatly *hypertrophied,* but sometimes normal or even contracted, and the seat of brown induration. The *kidney* is small and hard from overgrowth and contraction of connective tissue; the color is dark red, the surface granular, and the capsule adherent (*arteriosclerotic kidney*).

Describe the changes in the wall of an artery occurring in any form of aneurysm.

The earliest changes are due to atheroma and arteriosclerosis. The blood pressure being increased, the artery dilates at a point where it has been weakened by disease, and the wall undergoes compensatory thickening.

A *true* aneurysm is one consisting of all the coats of the vessel. A *false* aneurysm is one in which one or two of the coats are not represented; usually the wall consists of the adventitia. In a *dissecting* aneurysm the blood, after rupture of the inner coats, separates the intima and adventitia for a certain distance and breaks through the inner coat into the vessel, or through the adventitia into the surrounding tissues.

Define Marfan's syndrome.

Marfan's syndrome (arachnodactyly) is a generalized hereditary disorder of connective tissue affecting especially the bones (dolichostenomelia, arachnodactyly, pectus excavatum or carinatum), the eyes (ectopia lentis), the ligaments ("double-jointedness," dislocations, herniae, etc.), and the tendons (hypotonic muscles) and causing changes in the aorta (cystic medionecrosis) that may lead to valvular separation and insufficiency. Aneurysmal dilatation of the ascending aorta is common, and dissecting aneurysm or rupture is a frequent cause of death.

Give the sites and the pathology of varicose veins.

Dilatation of the veins occurs from mechanical obstruction to the circulation or from weakness of their walls. It is found more commonly in dependent portions of the body and is particularly frequent in veins of the legs, rectum, esophagus, neck of the bladder, spermatic cord, scrotum, and vagina. The veins become dilated, tortuous, and elongated. The walls of the dilated veins are usually considerably thickened.

What conditions may result from enlargement of lymph spaces or lymph vessels?

The term *lymphangioma* is applied to a tumor composed of dilated lymph vessels or lymph spaces; it may be capillary, cavernous, or cystic. *Macroglossia* is an enlargement of the tongue; *macrocheilia,* of the lips; *congenital cystic hygroma* ("hydrocele of the neck"); *nevus lymphaticus,* of the skin; *elephantiasis,* of the legs and scrotum.

THE LUNGS AND BRONCHI

Give the morbid anatomy of chronic bronchitis.

Congestion and fibrous thickening of the bronchial mucous membrane; sometimes it is atrophied and thin. Mucus is present in variable quantities. Disappearance of ciliated columnar epithelium.

Describe and give the pathology of congenital atelectasis.

Congenital atelectasis, or failure of the lungs to expand after birth, is due to general weakness, compression of the thorax, cerebral hemorrhage, or obstruction of the bronchus. The bases are chiefly affected. The lungs are dark red and the cut surface is smooth. Crepitation is absent and the tissue sinks in water.

Differentiate lobar, broncho-, suppurative, and interstitial pneumonia (pneumonitis) as regards pathology and etiology.

Lobar pneumonia is an inflammation of the air vesicles, with accumulation of cells, exudation, and *coagulation necrosis* of the exudate, with consolidation of one or more lobes, associated with an overlying fibrinous pleurisy. Commonest cause: *Diplococcus pneumoniae* (pneumococcus of Frankel).

Lobular pneumonia (*bronchopneumonia*) is also characterized by cellular proliferation and an exudate containing red blood cells and leukocytes, but unaccompanied as frequently by a pleurisy. Areas of consolidation in one or several lobules occur. Cause: Pneumococcus, usually in association with streptococcus or staphylococcus.

Suppurative or purulent pneumonia in the form of either a single abscess or of multiple abscesses or a purulent inflammation. *Single* abscess usually follows lobar pneumonia; multiple abscesses are due to aspiration of infected material, embolism, metastasis, or extension from suppuration in adjacent organs (mediastinum, pleura, bronchi, liver).

In *fibrous* or *interstitial pneumonia* permanent connective tissue is formed as a result of the cellular proliferation. It may be: (*a*) parenchymatous, due to the inhalation of irritants (pneumonoconiosis), or a termination of lobar pneumonia; (*b*) secondary, due to extension of chronic pleurisy, syphilis, healing of gummas, tuberculosis, or healing of a tuberculous process. *Interstitial pneumonitis,* following mild upper respiratory infections, migratory in character, involves the alveolar walls and peribronchiolar spaces, with less cellular infiltration than occurs in bronchopneumonia.

How does lobar pneumonia differ from bronchopneumonia in the microscopic characteristics of the exudate?

In *lobar pneumonia* the exudate contains fibrin, leukocytes, some red blood cells, and endothelial cells from the walls of the alveoli. The exudate undergoes coagulation necrosis.

In *bronchopneumonia* the exudate contains red and white corpuscles and epithelial cells, but less fibrin. There is no tendency to coagulation necrosis.

List the causes of death in Hamman-Rich syndrome (syndrome of alveolar-capillary block, interstitial pulmonary fibrosis).

Some cases of this disease have responded to steroid therapy but most do not. Death occurs from (1) progressive anoxia and respiratory failure, (2) intercurrent bronchopneumonia, and (3) cor pulmonale and right-sided heart failure.

Describe the lung in a case of pneumonoconiosis—"miners' consumption."

In a well-marked case the lung presents large areas of induration in which the vesicular structure of the organ is entirely destroyed. Fibrous bands accompany the bronchi and radiate in every direction toward the periphery. The fibrous tissue is sometimes arranged concentrically around a nucleus of silica dust. The lung is contracted, the pleura is drawn inward and thickened. The dark color of the affected areas is due chiefly to the coal dust but partly also to hemorrhagic pigmentation.

Define pulmonary alveolar proteinosis.

Pulmonary alveolar proteinosis is a recently recognized chronic disease of unknown etiology. The clinical course is variable. It may or may not begin with a febrile illness and usually has a prolonged course associated with dyspnea and cough. It is characterized by the filling of distal air spaces with a granular and floccular proteinaceous and lipid-containing material that stains positively with the PAS technique. This material appears to be derived from proliferating septal cells which become granular and undergo sloughing and necrosis. Acicular crystals and laminated bodies suggesting early stages of corpora amylacea may be present.

Mention the usual pathologic progression in pulmonary tuberculosis.

Invasion by tubercle bacilli, inflammation, formation of tubercles, encapsulation, and recovery, or secondary infection with pyogenic bacteria, suppuration and cheesy degeneration of the tubercles, and cavity formation.

Describe in detail the process of cavity formation in a case of tuberculosis of the lungs.

Infection with *Bacillus tuberculosis* first gives rise to the production of tubercles. As the lesions break down and finally undergo coagulation and liquefaction necrosis or caseation, the lung tissue is destroyed, and a cavity results. The cavity may grow by continued softening and cheesy degeneration of the walls, or fibrous tissue may be formed, encapsulating the cavity and arresting the spread of the tuberculous process. Sometimes the contents of a cavity undergo calcification.

Give the pathology of the different forms of pleurisy.

Fibrinous: Both surfaces of the pleura are covered with fibrin and yellow lymph, or there may be very little exudate (dry pleurisy). The pleura underneath is dry, opaque, and rough. Adhesions between the two layers and partial or complete obliteration of the sac are specially frequent in this form.

Serofibrinous: Acute pleurisy. The exudate contains much fibrin and pale yellow fluid that tends to coagulate. Flakes of lymph are found in the exudate.

Serous: The effusion is abundant and contains very little fibrin. This form is commonly tuberculous in origin.

Terminations of Pleurisy: Absorption, with a few slight adhesions; extensive adhesions or obliteration of the sac; suppuration or empyema.

Empyema (Pyothorax): The exudate is purulent. The condition may be tuberculous.

ABDOMINAL ORGANS

Give the pathology of peritonitis.

The peritoneum is injected, lusterless, and covered with lymph. The exudate in the peritoneal cavity is at first serous and may become fibrinous or purulent. Peritonitis tends to become localized by the formation of adhesions in the peritoneal cavity.

Compare the pathologic histology of tuberculous and traumatic peritonitis.

In *traumatic peritonitis* the membrane is injected, lusterless, and covered with fibrin and lymph. A small amount of serous or fibrinous exudate is present and adhesions are usually formed.

Tuberculous peritonitis is characterized by the presence of tubercles, which coalesce to form large masses. There is an abundance of serous exudate, and extensive fibrinous and fibrous adhesions are formed. In advanced cases the peritoneum is thickened.

Describe the pathologic characteristics of peptic ulcer.

Peptic ulcers are usually single and situated in the lesser curvature and in the posterior wall of the stomach, near the pylorus, or in the duodenum. The size varies from a few millimeters to 5 cm.; the shape is like a funnel with the apex in the muscular coat. The scars that result from healing of an ulcer have a characteristic stellate form. If they are extensive, pyloric stenosis or hour-glass contraction of the stomach may result.

Carcinoma of stomach: (*a*) Is it usually primary or secondary to carcinoma elsewhere? (*b*) Where is it usually situated? Give most common type.

(*a*) Usually primary. (*b*) It is usually situated at or near the pylorus in the lesser curvature, and the most common type is the adenocarcinoma.

Differentiate between a typhoid ulcer and a tuberculous ulcer of the intestine.

TUBERCULOUS

Chronic.
Long axis usually transverse.
Floor thickened and studded with gray tubercles. Gray tubercles around the ulcer and on serous coat.
Hemorrhage and perforation rare.

TYPHOIDAL

Acute.
Long axis usually longitudinal.
Floor thin; edges slightly undermined.
Hemorrhage and perforation not uncommon.

Give the pathology of uncinariasis.

Hookworm disease is caused by the presence in the intestines of *Necator americanus* or *Ankylostoma duodenale*, and the absorption of a toxin derived from the parasite, loss of blood, and probably secondary bacterial infection. The American variety of the species is called *Necator americanus.* The pathology of both forms is the same. There is profound *anemia* of the chloranemic type, with oligochronemia and a marked *eosinophilia.* Fatty degeneration of parenchymatous organs, heart, liver, and kidneys is the principal change observed post mortem.

Give the pathologic features of mechanical hyperemia of the liver (nutmeg liver).

The liver is large, the edges rounded, the color dark. The engorgement begins in the central veins, which on the cut surface appear deeply congested. Fatty infiltration or atrophy of the peripheral portions of the acini occurs secondarily. The contrast between the pale color of these portions and the dark, deeply congested central portions of the acini suggested the name "nutmeg liver." The *cause* of passive hyperemia is obstruction of the general circulation from cardiac or pulmonary disease, pleural effusion or thrombosis, or compression of the inferior vena cava.

Describe the pathologic histology of amyloid liver, and state where the deposit occurs.

The process begins in the subendothelial tissue of the walls of the blood vessels and between the endothelium of the sinusoids and liver cells, with resultant atrophy, but enlargement of the liver occurs if the deposit is excessive.

Give one classification of cirrhosis of the liver. Briefly discuss the various types.

Since the etiology of many forms of cirrhosis of the liver is obscure, classification is unsatisfactory. A great many names have been applied to various forms, including Laennec's, Hanot's, hemochromatosis or pigment cirrhosis, syphilitic cirrhosis, Banti's disease, and Wilson's progressive lenticular degeneration with cirrhosis. Because of the two main structures in the liver, a partially satisfactory classification may be based on them: namely, the portal system or liver cells, and the bile ducts or biliary system.

(*1*) *Portal Cirrhosis* (*Laennec's, atrophic, multilobular, alcoholic cirrhosis*): The etiology is uncertain. It appears to be a toxic reaction, the toxins acting on the liver cells, causing destruction and subsequent replacement with fibrous tissue. It is often, but by no means always, associated with chronic alcoholism. Recent therapeutic advances with high protein, high vitamin diets have suggested that it is due to a dietary insufficiency or poor ingestion of proper food, or that it is due to poor appetite resulting from excessive alcohol. Hemochromatosis may be included here.

(*2*) *Biliary Cirrhosis:* Less common than portal cirrhosis. It results from either obstruction of the bile ducts or infection. There is a progressive increase in dilatation and tortuosity of the bile ducts, increase in portal fibrosis, and a uniform staining of the entire liver with bile pigments.

Give the pathologic difference between yellow atrophy, amyloid liver, and portal cirrhosis (Laennec's cirrhosis).

Yellow Atrophy: The liver is small and soft, almost fluctuating; yellowish areas of fatty necrosis alternate with congested, red, hemorrhagic areas. Histologically, the principal change is patchy necrosis; the nuclei disappear, and the cells are filled with fat droplets. Blood pigment and cellular infiltration is present.

Amyloid Liver: The liver is uniformly enlarged and smooth, with rounded borders. The consistency is denser than normal, and the organ may pit on pressure. The color is "waxy" or "bacony." Microscopically the liver substance is translucent, cloudy, and grayish white. The nuclei are destroyed. With Lugol's solution the characteristic amyloid reaction —a dark, reddish-brown color—is obtained.

Portal Cirrhosis: The liver is hard and the surface irregular. It cuts with difficulty, revealing the hyperplastic bands of connective tissue around the lobules, which project from the cut surface. The color is not markedly altered. The liver cells are atrophied, particularly at the periphery of the acini; round-cell infiltration is conspicuous, and there is some proliferation of bile ducts.

Discuss the lesions seen in the liver in eclampsia.

Large hemorrhagic areas form the characteristic feature of the gross appearance. The microscopic picture is a combination of necrosis and hemorrhage. The necrosis is peripheral in type, being most marked around the portal vein. The etiology is unknown. The condition is seen during the last trimester of pregnancy or early puerperium.

Give the possible causes of occlusion of the bile duct.

Inflammation of the bile duct itself or of the duodenum; the presence of gallstones or parasites (ascaris, coccidia); pressure of a tumor, aneurysm, or floating kidney from without; malignant disease involving the duct; adhesions and cicatricial contraction.

Describe the pathogenesis of gallstones and the physical and chemical characteristics of one variety.

The formation of gallstones is attributed to two causes: (*a*) the presence of a nucleus—a mass of epithelial cells cast off from the walls of the bile duct, mucus, or a foreign body; and (*b*) change in the composition of the bile resulting from stagnation. The bile becomes inspissated and precipitates cholesterol, which is deposited around the nucleus and forms the stone. Bacteria are sometimes found in the center of the nucleus and represent the primary cause in some cases.

Most gallstones consist of the above-described nucleus and cholesterol, sometimes with an outer coat of bile pigment. The entire calculus may consist of biliary pigments in combination with calcium salts. Some calculi consist entirely of calcium carbonate.

What is an Eck fistula?

A fistula established artificially between the portal vein and the inferior vena cava so as to prevent the metabolic action of the bile upon the absorbed food.

Define pilonidal disease.

The adjective "pilonidal" is derived from the Latin terms *pilus,* meaning hair, and *nidus,* meaning nest. Pilonidal disease hence pertains to the clinical manifestations, usually inflammatory, of pilonidal cysts occurring in the sacrococcygeal region.

DISEASES OF THE GENITOURINARY ORGANS

Describe the structural changes in the condition of the kidney which frequently accompany chronic suppuration.

The *amyloid kidney* is enlarged, sometimes to double its size, harder than usual, and the cut surface is grayish or waxy, or mottled red and yellow. The process begins in the blood vessels of the tufts and spreads to the connective tissue but does not affect the cells. The capsule is thickened. Fatty infiltration of the epithelial cells develops sooner or later. The tissues give the amyloid reaction.

Briefly discuss the etiology of glomerulonephritis; mention its stages and the pertinent gross and microscopic picture of the kidney in each stage.

Glomerulonephritis is a condition closely associated with bacterial infection. Hemolytic streptococcal infections, such as scarlatina, streptococcus sore throat, tonsillitis, pharyngitis, furunculosis, erysipelas, and puerperal sepsis, have all been followed by glomerulonephritis. The disease does not occur until from 2 to 6 weeks after the onset of the infection and is not associated with a septicemia. In the vast majority of cases it develops after the initial infection has subsided. It is a sensitivity reaction primarily involving the glomerular capillaries.

(*1*) *First or Acute Stage:* Grossly the kidney is usually enlarged. The capsule strips easily, the surface is pale and covered with minute red dots. Microscopically the glomerular tufts are chiefly involved, with swelling of the glomeruli, so that they almost fill the capsular space. It is a very diffuse process involving almost all the glomeruli.

(2) *Subacute Stage:* The kidney is large, white, and smooth (but smaller than in acute stage). The microscopic picture suggests a transition between the further glomerular proliferation seen in the acute stage and the degeneration that appears later. Some of the glomeruli show marked glomerular caps or masses of cells between the capsule and the glomerular tufts. Others will be converted into structureless hyaline masses. Tubules show marked degenerative changes, with much fat in the cells.

(3) *Chronic Stage:* There is a small, white, scarred kidney with a capsule that strips with difficulty. Microscopically the end stage of degeneration is seen, with many hyalinized glomeruli and almost complete loss of normal renal structure.

Give the pathology of nephrosclerosis (arteriosclerotic kidney).

The *contracted kidney* is hard, small, red, and granular; the capsule is adherent. The cortex is very thin, the pyramids reaching almost to the surface. The blood vessels are markedly sclerotic; they project on the cut surface; the arterioles show hyaline thickening with narrowing of their lumina. The greater portion of the parenchyma is replaced by indurated fibrous tissue. Many of the glomeruli have disappeared, leaving only fibrous cicatrices, finely granular masses, or hyaline balls. Some tubules atrophy, the epithelium disappearing in many of them, while others become dilated.

Give the causes, pathologic findings, and effects on the organism of pyelonephritis.

Invasion of the kidney by bacteria, up the ureter from the bladder, through the peri-ureteral lymphatics, or by the blood stream—the more probable origin. The kidneys are enlarged, with small abscesses in the acute stage, with infiltration by polymorphonuclears in glomeruli and tubules. Healing leads to depressed scars, with an adherent overlying capsule, penetrating to the corticomedullary junction, and increased interstitial fibrous tissue with lymphocytic and plasmocytic cellular infiltration. Normal architecture is disorted in these areas and hyaline casts are frequent in the tubules. The findings in chronic pyelonephritis are a combination of the acute and healed, with greater destruction of parenchymal elements, both glomeruli and tubules, more fibrosis and thickening of the blood vessels, and small abscesses. The pelves may be partly necrotic, dilated, and inflamed in the acute stage and thickened and congested and containing exudate in the chronic stage. It is a frequent finding in hypertensive cardiovascular disease.

Classify and describe briefly the cysts of the kidney.

Most cysts of the kidney, from a simple cyst to the congenital cystic kidney, are due to a developmental error, or lack of union between convoluted and straight tubules. The usual classification is: (1) *retention cysts,* occurring in contracted kidney; (2) *solitary cysts,* supposed to be due to the coalescence of a number of small cysts; (3) *hydatid cysts;* (4) *congenital cystic kidney,* in which the kidneys may be very large and the parenchyma replaced by numerous large multilocular cysts; (5) *hydronephrosis,* a condition resulting from ureteral obstruction, and sometimes classified among the cysts of the kidney.

Define Peyronie's disease.

Peyronie's disease (plastic induration of the penis) is a common lesion of the fibrous coverings of the corpora cavernosa, usually involving the dorsal aspect and intercavernous system of these bodies. It appears as a painless plaque of fibrotic tissue similar to keloid formation and to Dupuytren's contracture of the volar tendons of the hand. In most instances the etiology is unknown but in some cases Peyronie's disease arises as a sequel to trauma.

Describe the structural changes of prostatic hypertrophy.

Uniform or nodular *enlargement;* usually the middle lobe or isthmus enlarges and presses upon the urethra. Microscopically the fibrous and muscular tissues are proliferated, producing induration and the appearance of fibromyoma of the uterus. Sometimes the *glandular portions* are chiefly involved and the appearance is that of adenoma. *Cystic softening* may occur.

Describe the pathologic changes one would expect to find in the urinary tract in a case of hypertrophy of the prostate of long standing.

Difficulty in the passage of urine with incomplete emptying of the bladder (residual urine) produces dilatation and hypertrophy of the bladder with increased intravesical pressure and retrograde dilatation of the ureter and kidney pelvis, producing hydronephrosis at the same time. The residual urine very frequently becomes infected, transmitting infection upward through the dilated ureters or periureteral lymphatics to the kidney proper, resulting in a pyelonephritis with multiple abscess formation. Not infrequently, vesical and/or renal calculi are also encountered.

DISEASES OF THE NERVOUS SYSTEM

Describe the pathologic conditions in meningitis.

The blood vessels are dilated, the arachnoid is edematous, and the cavity is filled with an effusion of serum, serofibrinous fluid, or pus.

Give the gross pathologic anatomy of cerebral apoplexy.

Rupture of one of the branches of a cerebral artery. The vessel is usually sclerotic and may be the seat of miliary aneurysms. The blood escapes into the brain substance and produces acute softening; the softened tissue may later be absorbed, so that a cyst or scar remains.

What conditions (nontraumatic) favor cerebral hemorrhage?

A high arterial tension and general arteriosclerosis, hypertrophy of the heart, miliary aneurysms of the cerebral vessels, brain tumor (increased blood pressure), leukemia, thrombocytopenia, and scurvy.

What vessels are most commonly involved in cerebral hemorrhage? In cerebral embolus?

The branches of the middle cerebral artery that supply the internal capsule, striate body, and optic thalamus, especially the *lenticulostriate artery.*

The artery of the sylvian fissure and, less frequently, the anterior cerebral artery.

Describe the local apperances in a case of embolism of the middle cerebral artery.

A thrombus is found occluding the vessel from the seat of embolism to the first collateral branch. Infarction, ending in cerebral softening (encephalomalacia), is usually present.

Give the causes and process of cerebral softening.

Causes: Hemorrhagic or anemic infarct, gradual compression by tumors, traumatism, and rarely toxins of tetanus and rabies.

Infarction: Results from obstruction of a cerebral artery by a thrombus or embolus. The wedge-shaped portion supplied by the occluded vessel becomes anemic, undergoes liquefaction necrosis, and may ultimately be replaced by a cyst or scar.

Mention the syphilitic lesions of the brain and of the spinal cord.

Brain: Gumma; diffuse endarteritis, with secondary sclerosis, paresis, and syphilitic meningitis.

Spinal Cord: Gumma; endarteritis, posterior sclerosis, and meningitis.

Where and what are the pathologic changes in bulbar paralysis?

A primary degeneration of the motor ganglion cells in the medulla, affecting the nuclei of origin of the facial, hypoglossal, spinal accessory, and vagus nerves.

List the common lesions involving the brachial plexus.

(1) Unilateral ruptured intervertebral disk; (2) foraminal spurs; (3) fracture dislocations and fractures of the lamina or facets; (4) stretch or avulsion of cervical nerve roots; (5) tumors; (6) Pancoast syndrome; (7) cervical rib; (8) scalenus anticus syndrome, and (9) stab or gunshot wounds.

Give the pathology of tabes dorsalis.

A primary ascending demyelination and degeneration of the axis cylinders of the posterior columns of the spinal cord, involving the whole of the column in the lumbar region. Higher up, the affected area is more median and, in the cervical portion, the column of Goll only is affected. Changes in the optic tract and oculomotor nerve and trophic lesions of the joints (arthropathies, Charcot joint) are also present.

Give pathology af acute anterior poliomyelitis.

Inflammation, round-cell infiltration, and intense congestion of the blood vessels in the anterior horn. Secondary interstitial changes in the gray matter, with cloudy swelling and, ultimately, destruction of the ganglion cells. As the neurogliar tissue increases, the anterior horn as a whole shrinks and becomes sclerotic. The degenerative process extends to the anterior roots and, later, the fibers of the motor nerve trunks become smaller and fewer in number. Atrophy of the muscles begins early and is well marked.

What part of the spinal cord is involved in progressive muscular atrophy?

The ganglion cells of the anterior horns and of the motor tracts, especially in the cervical region (the peripheral motor neuron).

Give some of the pathologic findings of general paralysis of the insane, or paresis.

Thickening of the meninges with cellular infiltration; edema of the pia; internal hemorrhagic pachymeningitis; increase of the cerebrospinal fluid; thickening and hyaline degeneration of the blood vessels (endarteritis) of the cortex; inflammation and degeneration of ganglion cells and proliferation of glial tissue.

METABOLIC DISTURBANCES

What are the usual pathologic lesions in diabetes mellitus?

There may be no demonstrable lesions in diabetes mellitus. By the use of special stains one can often demonstrate some hyalinization and degeneration in the islands of Langerhans. The changes may be most marked in the B cells of the islands of Langerhans.

Other lesions, such as arteriosclerosis, gallstones, intercapillary glomerulosclerosis, and increased susceptibility to skin and renal infections are secondary to the metabolic changes in diabetes rather than to pathologic lesions of the disease per se.

What is bronze diabetes?

Bronze diabetes or *hemochromatosis* is a rare disease thought to be due to a disorder of iron metabolism characterized by extreme hemosiderosis. The cause is unknown.

Hemosiderin is deposited in the skin giving it a bronzed tint. There is marked hemosiderosis in both pancreas and liver giving the pancreas a rich brown color, leading in both organs to a process of necrosis and fibrosis and resulting in marked functional disturbance. Diabetes mellitus associated with this condition may be severe and is notoriously unpredictable and difficult to manage. The disease is fatal. It may run either an acute course lasting for several months or a prolonged one lasting for one to four years.

Describe the pathologic conditions present in each of the forms of goiter.

Exophthalmic Goiter: Diffuse hypertrophy and increased vascularity, associated with exophthalmos and the classical symptoms of Graves' disease—tachycardia, spasm of the upper eyelid (widening of the fissure), twitching movements of the eyeballs, lagging of the upper lid during downward rotation (von Graefe's sign); tremors of the hand; general vasomotor disturbances (flashes of heat, serous diarrhea, etc.). Thyroid function is increased (hyperthyroidism) and basal metabolism above normal.

Colloid Goiter: The amount of colloid material in the gland is excessive and the tumor tends to degenerate. Areas of adenomatous tissue may be present (*nodular colloid goiter*). This type is also called "simple," "endemic," and "adolescent." Either there is no functional disturbance or a variable degree of hypothyroidism.

Cystic, fibroid, and calcareous degeneration may occur.

Adenomatous Goiter: Adenoma of the thyroid gland. It may be encapsulated (true adenoma) or nonencapsulated (adenomatosis). Areas of hypertrophy are often present both within the adenoma and in the surrounding thyroid tissue, and there is, in general, a tendency to degeneration. This type may be associated with either hypothyroidism or with hyperthyroidism (hyperfunctioning adenomatous goiter).

Myxedema: Physical or functional loss, or marked functional impairment, of the thyroid gland leads to myxedema, a metabolic disorder characterized by thickening of the subcutaneous tissues of the face, neck, and hands, due to the presence of a substance resembling mucin; tremor of the extremities; slowness of muscular movements and mental processes; and idiocy (cretinism).

What are some of the commoner manifestations of some of the deficiency diseases?

Beriberi: Polyneuritis (degeneration of myelin, fragmentation of axis cylinders, and Wallerian degeneration); dilatation of heart with myocardial degeneration; generalized edema (hypoproteinemia).

Wernicke's Disease: Degeneration of ganglion cells, dilatation of smaller blood vessels, and hemorrhage with glial formation in certain nuclei of the brain (thalamus, hypothalamus, midbrain).

Pellagra: Erythema and pigmentation of skin; acanthosis, hyperkeratosis and parakeratosis; inflammation of mucous membranes and atrophy of all internal organs; excessive pigmentation of the liver cells. The changes in the *anterior horns* of the cord are important. There is partial or complete dissolution of the fibrillae and atrophy of the nuclei, with *posterolateral sclerosis*. The posterior roots are not involved.

Scurvy: Petechial and larger hemorrhages into skin, muscles, and periosteum, producing pain and swelling in involved areas and gums; commonest in ribs, distal end of femur, and proximal ends of tibia and fibula; osteoporosis and deficient formation of dentine may result in loosening of teeth.

Rickets: Enlargement of junctions of cartilage and bone, in most rapidly growing areas of costochondral junctions ("rachitic rosary"), lower ends of radius and ulna and upper end of tibia, resulting from disorganized irregular proliferation of cartilage without regular calcification. The parathyroid glands are enlarged.

Osteomalacia: Occurs most commonly in adults, particularly females, more commonly in pregnancy and lactation, affecting the pelvic bones, vertebral column, and long bones of the lower extremities. There is loss of calcium and excess of osteoid tissue, with absence of clear definition between cortex and medulla. The parathyroids are commonly enlarged, due mainly to clear cells.

THE NASOPHARYNX AND LARYNX

Describe the changes in tissue in two forms of nasopharyngitis.

Chronic Hypertrophic Nasopharyngitis: The mucous membrane is swollen and reddened; the connective tissue, and sometimes the glandular and lymphatic tissue, are increased.

Atrophic Nasopharyngitis: There is atrophy of the mucosa, the normal constituents being replaced by connective tissue; the ciliated epithelium disappears and is replaced by squamous cells.

What are the causes of stenosis of the larynx? Give the pathology of stenosis of the larynx.

Edema of the laryngeal tissues, so-called "edema of the larynx" more correctly *edematous laryngitis,* is an inflammatory edema due to intense irritation, general or local infection, or tuberculous or syphilitic ulceration and perichondritis. The stenosis may be due to the presence of a *diphtheritic membrane.* Healing *syphilitic ulcers* cause contraction of the larynx. *Carcinoma* may produce stenosis.

Give the morbid changes taking place in acute edema of the glottis.

Edematous laryngitis is a true inflammatory edema, due to severe irritation or infection. The submucous tissue at the base of the epiglottis and over the aryepiglottic folds is greatly swollen and translucent or yellowish. The glottis is closed and asphyxia results unless the condition is relieved. Edema of the glottis may also be associated with severe allergic disorders.

THE EYE

What are the pathologic conditions in gonorrheal ophthalmia?

Suppurative conjunctivitis with intense chemosis and a free purulent discharge; swelling and edema of the lids; corneal ulceration; perforation of the cornea; anterior leukoma; anterior staphyloma; hypopyon; panophthalmitis or atrophy of the bulb.

Describe the pathologic lesions which may result from a spyhilitic or rheumatic iritis.

The iris is discolored and attached to the capsule of the lens by posterior synechiae; the pupil space may be covered with a false membrane, and in some cases inflammatory exudates are deposited in the anterior chamber. The condition is called *plastic iritis.*

Describe the changes that occur in the structure of the crystalline lens in cataract.

An opacity of the crystalline lens or its capsule or both, resulting from degeneration and vacuolation of fibers with gradual autolysis. Later, shrinkage may occur with calcification.

Give the pathology of retrobulbar neuritis.

Interstitial inflammation of the papillomacular fibers of the optic nerve.

What is retrolental fibroplasia?

An arrest of intraocular development, occurring in premature infants at birth, followed by an abnormal compensatory growth of fibrous tissue behind the lens and/or glial tissue associated with a detachment of the retina, frequently.

THE SKIN

What anatomic changes take place in the skin in chronic eczema?

Cellular infiltration of the corium and sometimes of the subcutaneous tissue, dilatation of blood vessels, hyperplasia of connective tissue, and enlargement of the papillae.

Discuss pigmentations of the body.

In a number of conditions colored materials are deposited in the skin or internal organs. There are two classes of pigmentations: (1) endogenous pigmentations, in which the colored substance is produced within the body—melanins, hemoglobin derivatives, and lipochromes; and, (2) exogenous pigmentations, in which the pigment is introduced into the body by way of the intestinal tract, skin, or lungs—silver, lead, carotene, and pigments used for decorative purposes (tattoos).

What pathologic conditions are present to cause an acne rosacea?

Dilatation of the blood vessels in the cutis, thickening and edema of the corium, marked hyperplasia of the connective-tissue elements of the cutis, and enlargement of the sebaceous glands.

Describe tuberculosis of the skin in any of its forms.

Lupus vulgaris is a chronic disease of the skin due to the tubercle bacillus and characterized by the development of brownish-red papules, tubercles, nodules, or infiltrated patches, which undergo absorption and ulceration and always leave scars. Lupus is a granuloma consisting of round-cell infiltration of the entire skin. Epithelioid, lymphoid, and giant cells make up the granulations. Tubercle bacilli in small numbers are found in the tissues.

Describe the causative agent and the production of the lesions of scabies.

The *Sarcoptes scabiei* is about 0.5 mm. long and two thirds as wide, with four pairs of legs, two on each side of the head, which is armed with suckers. The female, which is larger than the male, bores a burrow in the deeper layers of the epidermis after impregnation and there deposits her eggs. The young mites reach the surface of the skin, are in turn impregnated, and bore fresh burrows, thus keeping up the irritative and inflammatory process.

Section 3

CHEMISTRY AND PHYSIOLOGY

METABOLISM AND THE ENDOCRINE GLANDS

What is metabolism?

The power possessed by all living organized bodies of continually using up and renewing by chemical processes the matter composing their bodies. The process of building up is called *anabolism* or assimilation; the process of breaking down, *catabolism.*

The *objects* of metabolism are to build up new tissue and repair loss; to store up food material and fuel; to transform the food into heat and energy; and to prepare the excrementitious matters. The *chemical changes* consist in hydration, dehydration, reduction, and oxidation.

Give the metabolism of (a) proteins, (b) carbohydrates, and (c) fats.

(*a*) *Proteins:* These are acted upon by the *pepsin* and hydrochloric acid of the gastric juice and converted into *proteoses, peptones,* and *polypeptides.* When the chyme reaches the small intestine, the *trypsin* from the pancreatic juice continues the process of conversion into peptones and finally amino acids.

(*b*) *Carbohydrates:* These are acted upon first by the *ptyalin* in the saliva and converted into *maltose.* This action continues for a short time in the stomach until it is arrested by the acid reaction, to be resumed in the intestine, where the chyme is acted upon by the *amylopsin* of the pancreatic juice and also by enzymes secreted by the small intestine, which complete the conversion of carbohydrate to absorbable monosaccharides.

(*c*) *Fats:* These are split up into fatty acids and glycerin and formed into soaps and emulsions. This process takes place in the intestine under the influence of steapsin from the pancreatic juice, assisted by the bile.

Define nutrition.

A process which results in a state of nourishment of the various cells of the body. This state is dependent on certain nutritional factors—namely, nonspecific substances used for energy production, growth and repair (carbohydrate, fat, protein), and specific substances that are not synthesized by the body in adequate amounts (iron, iodine, certain fatty and amino acids, vitamins, provitamins, water, and oxygen.

Discuss the role of protein metabolism.

Protein metabolism includes practically all of the physiological processes of the body. Tissue growth and repair are dependent upon protein; hemoglobin is an important protein; the hormones, enzymes, and antibodies are protein products. Protein affects water balance through its oncotic pressure as well as by its participation in acid-base balance.

List the essential amino acids in the diet.

The protein molecule consists of 23 amino acids, and the various proteins contain these units in varying amounts, numbers, and combinations, so that the molecular weights of proteins vary accordingly. Of the amino acids which make up proteins, at least ten are essential in the diet because of inadequate synthesis by the body: arginine, histidine, isoleucine, leucine, lysine, methionine, phenylamine, threonine, tryptophane, and valine. The other amino acids are produced in the body: alanine, glycine, glutamic acid, etc. Arginine can be synthesized, but at an insufficient rate.

Does the human body store protein?

Yes. Protein is stored in the form of labile or deposit protein in all tissues including the plasma. This is drawn on in starvation. On a normal diet these proteins form a reserve (metabolic pool).

What becomes of the nitrogen ingested with the food?

Almost all is excreted in the urine in the form of urea; about 2 per cent as uric acid and creatinine, and from 4 to 5 per cent in the feces. Traces escape with the expired air.

What is meant by nitrogen balance?

The difference between the nitrogen ingested in food and that excreted in urine and feces is the nitrogen balance. Negative nitrogen balance is found in starvation, postoperatively, and during infections when the intake of food is not sufficient to replace protein necessary for the body. Nitrogen balance is found in health when the intake equals the output (except in children when intake exceeds output to provide for growth).

What is meant by the protein-sparing effect of carbohydrate and fat?

A starving person will excrete almost three times as much nitrogen as a person on a protein-free diet containing adequate caloric requirements of fat and carbohydrate. Hence carbohydrate and fat prevent rapid breakdown of proteins in the body. Carbohydrate has a marked protein-sparing action. Fat has only a slight protein-sparing action.

Discuss the fractionation of plasma proteins based upon electrophoresis.

By electrophoresis, the proteins may be grouped into three large fractions: albumin (two groups), globulin (alpha, beta, gamma), and fibrinogen. These fractions may be further subdivided—for example, gamma globulins, representing a number of different immune bodies. Fractionation is used both as a diagnostic procedure and therapeutically (purified albumin for certain deficiency diseases, gamma globulin for passive immunity, etc.).

What factors influence the biological value of proteins?

(1) The amounts and relative properties of their constituent amino acids. The dietary requirement for protein is really a requirement for amino acids, some of which (essential amino acids) cannot be synthesized by the organism from substances ordinarily in the diet at a rate commensurate with certain physiological requirements (optimal growth of the young and maintenance of nitrogen equilibrium in adults). Also, food proteins vary considerably in the efficiency of their utilization for synthesis of body proteins with animal proteins

(egg, milk) generally of higher quality than those of vegetable origin. Hence, the diet must provide "essential" amino acids that cannot be synthesized by the body as well as adequate amounts of high quality proteins.

(2) The nutritional availability (rates of liberation and absorption) of their amino acids under conditions of digestion in the gastrointestinal tract. The digestibility of various proteins and the rates of release of amino acids may be affected adversely or beneficially by the manner of commercial processing or preparation of foods by heat. Furthermore, if a low quality protein food, such as white bread (low in lysine) is supplemented by potatoes (adequate in lysine) its biological value is doubled. Similarly, the utilization of relatively low quality vegetable proteins is enhanced by the addition of a high quality animal protein. Finally, if a protein molecule is to be synthesized, all of its constituent amino acids must be available simultaneously in proper amounts. (If an interval of longer than one hour is allowed to elapse between ingestion of an incomplete amino acid mixture and administration of the missing essential amino acid, these amino acid constituents are not utilized for protein synthesis.) Hence, the importance of proper processing and preparation of foodstuffs and a balanced diet distributed evenly throughout the three daily meals.

What essential substances draw upon the amino acid pool for their formation?

Such essential substances as enzymes, plasma proteins, hemoglobin, purines and pyrimidines (i.e., nucleotides and nucleic acids), creatine, glutathione, and certain hormones (e.g., insulin, epinephrine, thyroxine, anterior pituitary, and parathyroid hormones).

Discuss the influences of hormones in protein metabolism.

The synthesis and degradation of proteins are markedly influenced by certain hormones:

(*1*) *Growth Hormone:* This exerts a protein anabolic effect, with a diminished urinary excretion of nitrogen (positive nitrogen balance) and increased deposition of protein in tissues.

(*2*) *Androgenic Hormones:* Testosterone exhibits a protein anabolic effect with a decrease in excretion of urinary nitrogen and stimulation of somatic growth in prepubertal children, increased weight, etc.

(*3*) *Adrenocortical Hormones:* 11-Oxygenated adreno-corticosteroid hormones exert a protein catabolic effect—increased urinary excretion of nitrogen (negative nitrogen balance)—which is intimately related to their action in increasing gluconeogenesis.

(*4*) *Insulin:* This is necessary for the protein anabolic effect of growth hormone (1) and antagonizes the gluconeogenic action of adrenocortical hormones (3).

(*5*) *Thyroxine:* This exerts a protein anabolic effect, especially in the growing organism.

Give the relative food value and ease of digestion of meat, milk, eggs, and leguminous fruits.

According to relative food value, the order is: meat, eggs, milk, and leguminous fruits. According to relative ease of digestion, the order is: milk, eggs, meat, and leguminous fruits.

What role do the nucleic acids and their derivatives play in body metabolism?

The chief role of nucleic acids and their derivatives appears to be in the control of the general pattern of metabolism: namely, chromosomes consist largely of deoxyribonucleic acid (DNA, "genetic material") and protein; several plant viruses have been shown to be crystallizable nucleoproteins, and many animal viruses are largely nucleoprotein; deoxyribonucleic acid appears to be the active agent ("transforming substance") that endows certain strains of *Pneumococcus* with the capacity for synthesizing an enzyme that it did not previously possess which, in turn, catalyzes the formation of the type-specific capsular polysaccharide. In addition, the nucleic acids and their derivatives have catalytic functions and act in conjunction with enzyme systems—the adenylic acid system that is intimately associated with the energetics of all living cells, and the coenzymes, which certain enzymes require for their function, contain nucleotide units or are structurally related to them.

What factors influence the abnormal amounts of urea nitrogen in the blood?

(1) Decreased renal excretion of urea due to organic disease of the kidneys with destruction of a considerable portion of functioning renal tissue—kidney diseases (acute and chronic glomerulonephritis, nephrosclerosis, tuberculosis, pyelonephritis, malignancy, blockages of uriniferous tubules by sulfonamide crystals or free hemoglobin, renal conditions accompanied by marked oliguria or anuria, as bichloride poisoning, lower nephron nephrosis, and others); or (2) abnormality of the mechanism of glomerular filtration resulting in significant decrease in the effective filtration pressure (increased capsular pressure [lower urinary-tract obstruction], marked hypotension, hemoconcentration, hyperproteinemia).

Define creatine and creatinine.

Creatine is derived from glycine, arginine, and methionine and is of fundamental importance as phosphocreatine in the phenomenon of muscle contracture. The capacity of the muscles for contraction is related to their phosphocreatine content, the force of contraction is proportional to the extent of breakdown of the latter, and restoration of excitability in the muscle after contraction is dependent upon resynthesis of the hydrolyzed phosphocreatine. Creatine is present in the blood almost entirely in the erythrocytes, is completely reabsorbed in the renal tubules at low concentrations, but appears in the urine when its plasma concentration exceeds 0.6 mg. per 100 cc.

Creatinine, a waste product of creatine, is therefore usually of endogenous origin with the amount eliminated in urine serving as an index of the level at which the body maintains its phosphocreatine level. (The amount of creatinine excreted in a twenty-four hour urine collection corresponds to about 2 per cent of creatine in the body.)

Define agammaglobulinemia.

A condition in which there is an absence or extremely low levels of gamma globulins in the serum, an inability to respond to artificial immunization with the production of circulating antibodies, absence of isohemagglutinins, history of recurrent bacterial infections, failure of prolonged antimicrobial therapy to furnish protection and a satisfactory response to protective injections of gamma globulin.

Discuss uric acid metabolism.

Although the exact site of uric acid formation is not known, its ultimate production may be influenced by factors that affect the metabolism of protein, carbohydrate, and fat, as well as those affecting the degradation of exogenous and endogenous nucleic acid and nucleotides. After formation, uric acid passes into the blood stream and is excreted largely in the urine, with about 90 per cent of that which enters the glomerular filtrate being reabsorbed in the renal tubules. This latter mechanism is of importance in connection with the action of certain uricosuric agents—cinchophen, salicylates (large doses), and Benemid—which greatly increase urinary elimination of uric acid by inhibiting its reabsorption in the renal tubules, presumably by blocking the enzymatic transport mechanism. Also, ACTH and the cortisone group of drugs increase the urinary excretion of uric acid, although it is not certain whether this is due primarily to tubular inhibition or to stimulation of purine metabolism. The blood uric acid is normally little affected by the ingestion of purine-rich foods whereas the amount excreted in the urine varies with the purine (nucleoprotein) intake.

Discuss the causes of hypoalbuminemia.

Decrease in plasma albumin concentration may result from: (1) loss of albumin, prolonged albuminuria (nephritis, nephrosis), ascites, excessive burns, severe hemorrhage, polyserositis (Peck's disease), intestinal obstruction, generalized peritonitis, etc.; (2) inadequate supply of protein, inanition, gastrointestinal disorders impairing protein digestion or absorption—prolonged vomiting or diarrhea (gastrointestinal cancers, steatorrhea, pellagra, etc.); (3) impaired synthesis of protein—chronic liver disease, infections, severe anemias, pregnancy and lactation, etc.; (4) excessive breakdown of body protein—uncontrolled diabetes mellitus and severe thyrotoxicosis; and (5) plasma dilution —administration of large quantities of solutions of sodium salts or a sudden dilution of the plasma such as follows an acute, massive hemorrhage.

Discuss the mechanisms which underlie the development of porphyria and porphyrinuria.

Porphyria designates those conditions characterized by the excessive production and excretion (porphyrinuria) of porphyrins and/or a precursor, porphobilinogen, as a result of certain factors: (1) an accelerated rate of synthesis of heme (hemolytic anemia), which results in the formation and excretion of excessive amounts of type-I porphyrins; (2) interference with the synthesis of heme, which gives rise to an accumulation and excretion of excessive amounts of type-III porphyrins; and (3) impaired liver function or biliary obstruction in the absence of an "inborn error" in porphyrin metabolism resulting in increased amounts of coproporphyrin I in the urine.

What are the chief dietary sources of carbohydrates?

Of the many polysaccharides existing in basic foodstuffs, only a few are of importance, namely, starches, dextrins, and glycogens, derived from grains and tuberous and leguminous vegetables, which make up approximately half of the usual carbohydrate intake. The other half consists of foods containing monosaccharides or disaccharides, namely, sucrose (granulated sugar, molasses, maple syrup), lactose (milk products), maltose (malt products), and glucose and fructose (fruits, honey, and corn syrup). In addition, potential carbohydrate results indirectly from conversion of protein and fat to carbohydrate intermediates, about 50 per cent of protein and 10 per cent of fat being theoretically available for such purpose.

Define the following terms: (1) gluconeogenesis, (2) glycogenesis, and (3) glycogenolysis.

(1) *Gluconeogenesis:* the formation of carbohydrate from molecules that are not themselves carbohydrates, as protein and fat. (2) *Glycogenesis:* conversion of glucose to glycogen. (3) *Glycogenolysis:* hydrolysis of glycogen to glucose.

How is carbohydrate stored in the body?

The total potential carbohydrate is small, practically all being stored in the liver and muscles and transported to all tissues as glucose, approximately two thirds of which is present as muscle glycogen; before it can be utilized it must be broken down to lactic acid and resynthesized to glycogen in the liver. The hepatic stores of carbohydrate, which constitute the only immediately available source of circulating glucose, are so small that, were they called upon to supply the entire energy needs of the body, they would last only a few hours. Thus, a regular intake of carbohydrate is necessary if breakdown of body proteins for gluconeogenesis is to be avoided.

Discuss the regulatory mechanism of carbohydrate metabolism.

The most important role in the regulation of glucose metabolism is played by the liver in that it represents the only direct source of blood sugar. The pancreas produces at least two substances, insulin and glucagon, which alter the blood-sugar levels in opposite directions. In addition, other endocrine glands produce a number of hormones that directly or indirectly affect the metabolism of carbohydrates, such as pituitary (adrenotropic, thyrotropic) adrenal cortex, and thyroid. However, the liver remains immediately responsible for the level of the blood sugar at any given time, as it is here that glyconeogenesis, glycogenesis, and glycogenolysis occur in response to variations in external supplies and internal stores of carbohydrate and changing levels of hormone activity.

Describe the energy or heat-producing value of food principles.

The unit is the *calorie* or amount of heat required to raise the temperature of 1 kg. of water from 0° to 1°C. The heat value of carbohydrates is equal to 4 calories per gram; fats, 9 calories; proteins, 4 calories per gram. If the relative proportions of alimentary principles in a given food are determined by analysis, the fuel value of the food can be calculated.

What is the respiratory quotient? Discuss its significance.

The respiratory quotient is the direct ratio of the quantity of carbon dioxide expired to the quantity of oxygen inspired in a given period of time (one minute). It is a measure of the metabolic activity of the body. If pure carbohydrates are burned, theoretically the R. Q. is 1; if pure fats, it would equal 0.7; the R. Q. of proteins is 0.8. The R. Q. is low in diabetes mellitus and in alkalosis; it is high during exercise and in acidotic states.

Discuss the mechanisms whereby work in heat becomes tolerable.

The ability for man to work effectively in heat is dependent upon physical fitness for the task, which includes an adequate physical structure, salt and electrolyte balance, hydration, proper motivation, acclimatization, and the relative heat and work loads.

What factors are involved in the heat load and the basic heat equation?

The heat load consists of internal (metabolic) body heat that is generated by oxidative processes and environmental (climatic) heat, which comes from the sun and warms the earth, air, and man. The effects of heat in the air are dependent on its capacity of convection and are influenced by moisture content as a result of its influence on evaporation. The basic heat equation constitutes the factors that are involved in governing the heat regulation of the body—namely, body metabolism, mechanical work done, evaporative heat loss, radiation (gain or loss), convection (gain or loss), conduction (gain or loss), and ingesta, excreta, or unevaporated sweat (gain or loss). Excessive heat may result in heat exhaustion, heat stroke, heat cramps, and thermogenic anhidrosis and, although the mechanisms differ, they all result from the disparity between the internal (metabolic) plus environmental (climatic) heat load and the capacity for eliminating heat.

Give the origin of normal fat in the human body and name examples of the types of food from which it is elaborated.

The normal fat of the body is derived in part from the non-nitrogenous moiety of proteins, and from the fat and carbohydrates ingested. The body fats function chiefly as a source of easily stored energy and play an active part metabolically, being available for carbohydrate and protein synthesis.

Define the following: (1) phospholipids, (2) steroids, and (3) lipoproteins.

(*1*) *Phospholipids:* The most important members of this group are lecithins, cephalins, and sphingomyelins and they are the dominant type of lipid in tissues other than adipose. It is probable that the phospholipids participate in the lipoprotein complexes, which are believed to constitute the matrix of cell walls and membranes; certain enzymes appear to require tightly bound phospholipid for their action; substances having the properties of phospholipids are believed to function as part of both thromboplastin and antithromboplastin in the mechanism of blood coagulation and may play some role in the aggregation of lipoproteins and in the metabolism of fatty acids.

(*2*) *Steroids:* This term is applied to a large group of compounds having in common a structure based on the cyclopentanophenanthrene nucleus. Included in this group are the following substances, which have greatly diversified physiological properties: bile acids, hormones (adrenocortical, androgens, estrogens, progesterone), and certain carcinogens. In addition, there are some steroid alkaloids, cardiac glycones (genins) and steroid sapogenins (gitonin, digitonin, and tigonin).

(*3*) *Lipoproteins:* These are combinations of lipids with protein in the tissues and are widespread throughout the body. Most of the lipid in blood serum (as well as the lipid-soluble vitamins, the carotenoids, and the steroids) is carried in the form of lipoprotein complexes. The thromboplastic protein isolated from the lung has been characterized as a lipoprotein.

Do foods contain nutritionally deleterious components?

Yes. Certain foods contain toxic materials, as a result of either processing or natural occurrence. These include such factors as lead, silenium, and copper; fava beans may induce a hemolytic disorder (favism); soybeans contain a principle with antitryptic activity, which depresses appetite and interferes with protein digestion, an effect similar to that of gossypol in cottonseed oil.

Define emulsification and saponification. Illustrate.

Emulsification is the breaking up of fat into very small particles and holding them in suspension in a liquid in which they will not dissolve, as mixing together oil and water. Saponification is the replacing of the glycerin of a fat by an alkali, as the mixing of olein and sodium hydrate to form sodium oleate and glycerin.

Discuss the metabolism of cholesterol.

The liver represents the major site of synthesis of cholesterol and is the chief source of esterified (60 to 80 per cent) as well as of free cholesterol (20 to 40 per cent) of the blood plasma (140 to 260 mg./100 cc.), although active synthesis may occur in many other tissues, such as arterial walls, which is of interest in connection with atherosclerosis. The rate of synthesis is influenced by the supply of dietary cholesterol, diabetes mellitus, thyroid dysfunction, etc. Cholesterol is excreted through the intestinal wall into the large intestine and via the bile into the small intestine.

What are the subjective untoward effects of an excessively high fat intake?

An excessively high fat intake produces anorexia and gastric distress, as a result of inhibition of gastric secretion and motility, whereas intestinal irritation and diarrhea may result from excessive amounts of fatty acids in the intestine.

Discuss the mechanism involved in the thymol turbidity and cephalin-cholesterol flocculation tests.

In general, these tests are based on the observation that certain qualitative reactions yield abnormal results in the presence of abnormalities in one or more plasma globulin fractions. The addition of thymol solution to certain sera with an abnormally high globulin content results in marked turbidity of the solution, whereas little or no such reaction occurs with normal serum. When a diluted serum with an abnormally high globulin content is added to an emulsion of a cephalin-cholesterol mixture, the latter substances precipitate out (flocculation) and the solution is clarified (opalescence decreases).

What is the composition of human milk?

Milk contains 112 parts of solid matter to the thousand. Of these, 60 parts are the carbohydrate lactose; 30 are fats: olein, palmitin, stearin, and butyrin; 20 are proteins: casein, lactoglobulin, and lactalbumin; and 2 parts are salts, especially sodium chloride and calcium phosphate.

Water	87.4
Total protein	2.3
Fat	3.8
Sugar	6.2
Salts	0.3
	100.0

Give the approximate composition of these following foods: egg, white bread, milk, beef steak, spinach, lima beans.

	PROTEIN PER CENT	CARBOHYDRATE PER CENT	FAT PER CENT	CALORIES PER 100 GM.
Egg	13	0	10	148
Bread	10	64	1.3	310
Milk	3.3	4.8	4.0	68
Steak	19	0	20	247
Spinach	2.3	3.2	0.3	20
Beans	4.0	13	3	97

What common foods contain the proteins ingested in the average American diet?

Eggs, meat, milk, wheat, corn, rice, peas, beans.

What is the specific dynamic action of food?

Ingestion of food will raise the basal metabolism. Protein causes the greatest rise, fat the least. It is wasted energy. The exact mechanism causing it is unknown.

What is the basal metabolic rate?

It is the term applied to the heat production of a subject who, though awake, is as nearly as possible at complete mental and muscular rest and in the postabsorptive state. It is most commonly calculated by the oxygen consumption in the resting state. The respiratory quotient is assumed to equal 0.82 and with this value the caloric equivalent of a liter of oxygen may be calculated. The basal metabolic rate is expressed as calories per square meter of body surface.

Discuss the effect of the cooking of food as a means of rendering it more digestible.

In general, cooking softens the food so that it can be masticated and more easily digested; destroys all parasites and disease germs that may be present; and develops certain flavors that increase the appetite and add to the enjoyment. It destroys the tough fibrous envelopes that surround many foods. On starchy food cooking acts by breaking up the cellulose covering of the starch granules, so that they can be more readily acted upon by the various digestive fluids, and by changing some of the starch into dextrin. The effect of cooking on proteins is to cause coagulation and to develop savory odors and flavors from the various extractives. Proteins are not always benefited by cooking, uncooked albumin being sometimes more readily digested than coagulated cooked albumin, as, for example, in the case of eggs.

What physiologic processes depend upon an adequate supply of minerals?

(1) Maintenance of pH at proper levels, (2) maintenance of osmotic pressure, and (3) the formation of body framework.

Discuss the mechanism of mineral deficiency.

The usual cause of a mineral deficiency is an inadequate amount of certain minerals in the food, namely, iodine, sodium, calcium, phosphorus, iron, and fluorine. Others, however, abound in nature and are required in such small amounts that deficiency is unusual (zinc, aluminum, magnesium, cobalt, nickel, copper). In addition, such conditions as faulty absorption, impaired utilization, or excessive loss of any of the minerals will cause a mineral deficiency state.

Mention some of the important functions of body calcium.

(1) Decrease of neuromuscular excitability, (2) decrease of capillary and cell membrane permeability, (3) necessary for normal muscle contraction, (4) necessary for normal transmission of nerve impulses, (5) essential for blood coagulation, and (6) activation of certain enzymes.

What factors influence the absorption of calcium?

Calcium is absorbed in the small intestine, the amount depending somewhat on its concentration in the intestine and the requirements of the body for calcium. Since the calcium salts are quite soluble in acid solutions and are relatively insoluble in alkaline solutions, factors that increase intestinal acidity favor absorption of calcium (organic acids—lactic, citric, amino and fatty acids). Other substances in food mixtures, such as vitamin D, promote absorption of calcium, whereas an excess of magnesium may diminish its absorption, especially if calcium is not present in adequate amounts.

Discuss the regulation of iron by the body.

Unlike most other electrolytes, the quantity of iron in the body is controlled by its absorption into the organism, rather than by regulation of its excretion. Absorption occurs chiefly in the upper duodenum and stomach. On entering the mucosal epithelial cell, ferrous iron is oxidized, forming ferric hydroxide, which combines with the protein apoferritin, synthesized in the cell, forming ferritin. Since iron ceases to enter the cell when its storing capacity of ferritin is exhausted, the amount of ferritin in the mucosal cells thus regulates iron absorption from the gastrointestinal tract. After ingestion, the iron passes into the blood plasma, undergoes reversible changes, combines in the ferric state with one of the plasma beta-globulins to form "siderophilin," and is carried to the tissues where it is utilized or stored as ferritin (the liver, spleen, and intestinal mucosa being the chief storage sites). Mobilization of iron from ferritin in storage sites is accomplished by reversal of the reactions involved in its storage. In general, ferrous iron is better absorbed than ferric, and the absorption of inorganic salts of iron compares favorably with that of the iron of foodstuffs, which is chiefly a colloidal ferric hydroxide. Regardless of the form in which iron is ingested, its absorption is interfered with by the administration of alkalis and by achlorhydria.

What disturbances may result in a deficiency in iron?

A decreased formation of hemoglobin, decrease in circulating hemoglobin, abnormalities in the serum iron concentration, or abnormal deposition of iron-containing pigment (hemosiderin) in the tissues.

Discuss the protein content of fluid in the tissue spaces and serous cavities.

Normally, the fluid in tissue spaces and serous cavities contains practically no protein as compared with that of blood plasma, because of the relatively poor diffusibility of protein through normal capillaries. However, in inflammatory processes or exudates the protein content is relatively high, as a result of an increased permeability of the capillaries in the involved area (empyema, purulent meningitis, etc.). In contradistinction to the high protein values in inflammatory fluids, the protein content of noninflammatory edema fluids or exudates (pleural effusion and ascites due to cardiac failure, nephrosis, etc.) is low, since they occur independently of alterations in capillary permeability.

Discuss the various exchange systems between the fluid compartments of the body.

The continued entrance of substances into the body from without (water, oxygen, organic and inorganic foodstuffs, etc.) and the production of metabolites from within, many of which must be distributed to other tissues or be excreted, result in a continual movement of the various components across the capillary and cell wall membranes of the body fluid compartments by certain exchange systems. Alveolar air: blood plasma—provides for entrance of oxygen into and loss of CO_2 and water from the body. Plasma: erythrocyte—permits exchange of oxygen, CO_2, water, and certain anions (particularly Cl^- and HCO_3^-) in both directions. Plasma: interstitial fluid—these being separated by capillary walls, which are permeable to water, inorganic ions, and small organic molecules (glucose, amino acids, etc.) but not to large organic molecules (proteins). Interstitial fluid: intracellular fluid—these being separated by cell membranes, across which gases, water, and small unchanged molecules can diffuse readily, whereas cations or anions and large molecules (proteins) diffuse less freely except in special situations.

Contrast intracellular and extracellular body fluids.

Approximately 50 per cent of the water in the body is confined within the cells as intracellular fluid. Of the remaining fluid, approximately 20 per cent lies outside of the cells; this is called the extracellular fluid, and it is composed of: (1) intravascular fluid (blood and lymph), and (2) interstitial fluid occupying the tissue spaces. In general, the composition of the solution within these fluids is strikingly different; in intracellular fluid, potassium represents the predominant cation and phosphate and protein the chief anions; whereas in extracellular fluid, sodium is the primary cation and chloride and bicarbonate the primary negative ions.

Give the principal causes of acidosis and alkalosis.

Acidosis: (1) Ingestion of acid, (2) reduced elimination of carbon dioxide due to functional insufficiency of lungs, (3) increased formation of acids as occurs in diabetes, and (4) loss of base by way of kidneys or gastrointestinal tract.

Alkalosis: (1) Ingestion of base, (2) excessive loss of carbon dioxide due to hyperventilation of central origin or altitude, and (3) loss of acids as in vomiting and/or intubation.

To which fundamental physiologic processes are sodium, potassium, and chloride related?

The maintenance of: (1) normal water balance and distribution, (2) normal osmotic equilibrium, (3) normal acid-base equilibrium, and (4) normal neuromuscular irritability.

What are the principal uses of water and list the routes of its intake and loss.

Water is essential to life. It is a constituent of all tissues and fluids of the body, distributes the nutriment, removes waste matters, and conveys them to organs of elimination. Under normal conditions, water is taken into the body through the gastrointestinal tract and lost by evaporation from the skin and respiratory surfaces and by excretion as a liquid in urine, sweat, and feces.

What points should be considered in the clinical evaluation of water balance?

(1) Record of intake and output, (2) measurement of abnormal loss of secretions—vomitus, drainage, etc., (3) initial body weight, and (4) general state of the patient—hypotension, hemoconcentration, oliguria, azotemia, etc.

Discuss potential fluid spaces.

A potential fluid space is one that normally contains little or no fluid but under abnormal conditions can accumulate very large quantities of fluid. These spaces include: the intrapleural space, the pericardial space, the peritoneal cavity, the joint spaces, and the bursae. The same conditions that cause edema in the interstitial spaces can cause fluid to collect in the potential spaces. An especially important cause of large quantities of fluid in a potential space is infection. Such an infected fluid is called an exudate, while fluid that simply collects because of abnormal capillary dynamics is called a transudate.

Define edema and discuss some of the factors concerned with its pathogenesis.

Edema consists of a localized or generalized accumulation of extracellular fluid. In general, two conditions produce edema. (1) One is some disturbance of the normal exchange fluid and solutes across the capillary wall. This represents the fundamental cause of most types of edema. Examples are: (a) increased capillary blood pressure—congestive heart failure, thrombophlebitis, external pressure on veins, dependency, etc.; (b) decreased colloid osmotic pressure—loss of albumen (ascites, etc.), inadequate protein intake (dietary restrictions, etc.), impaired synthesis of plasma protein (infection, etc.); (c) increased capillary permeability—inflammation, anemia, etc.; (d) decreased lymphatic drainage—lymphedema, increased venous pressure. (2) The other is a fundamental defect in sodium and water excretion, which is characterized by increased renal reabsorption of sodium, chloride, and water. This mechanism represents a primary factor in the pathogenesis of renal edema—increased sodium reabsorption by the renal tubules. In addition, certain hormones similarly produce edema—namely, adrenocorticoids (cirrhosis syndrome), estrogens, and progesterone (premenstrual edema).

What are vitamins?

Vitamins are chemical compounds of highly diversified structure that must be present to allow for normal function and reproduction of an organism. Vitamins or their derivatives act as coenzymes in a large number of metabolic reactions. Vitamins are often present in or synthesized by plants and bacteria, and most of the human supply of these factors comes from eating plants or other animals or from bacteria in the normal intestine. Formerly, vitamins were usually designated by letters. The present trend is to use a specific name, such as thiamine instead of vitamin B_1. Deficiency of the various vitamins in the body gives rise to a series of deficiency diseases, the avitaminoses. The vitamins are often divided into two groups: fat-soluble vitamins, including A, D, E, and K; water-soluble vitamins, including thiamine, riboflavin, niacin, ascorbic acid, pyridoxine, pantothenic acid, biotin, folic acid, and cobalamin.

How do the following vitamins function: (1) vitamin A, (2) thiamine (vitamin B_1), and (3) ascorbic acid (vitamin C)?

(1) *Vitamin A* functions primarily by stimulating the development of new cells and joins with the protein to form visual purple. These two actions explain the clinical manifestations associated with its deficiency: night blindness, xerosis, xerophthalmia, dermatitis, vaginitis, etc. (2) The signs and symptoms associated with *thiamine* (*vitamin B_1*) deficiency result in part from involvement of the peripheral (and possibly the central) nervous system. The clinical picture of neuritis may be present, however, even though the myelin sheath is normal. This may be explained by the fact that nervous tissue utilizes only glucose for energy, and, since thiamine is an essential factor in pyruvic acid metabolism, an absence of an adequate supply of thiamine will result in a decreased oxygen uptake. In other words, this disturbance in the metabolism of nervous tissue might cause functional changes and, if sufficiently severe and continued long enough, would result in structural damage. Whether similar change in the cardiac nerves accounts in part for the cardiovascular changes is not clear. (3) The principal defect associated with ascorbic

acid (vitamin C) deficiency is the failure of formation of normal connective tissue, especially in bones, tooth structures, and healing wounds. The hemorrhagic manifestations are considered to be secondary to increased capillary fragility.

What common foods contain the following vitamins?

Vitamin A: Green vegetables, carrots, milk, eggs, butter.

Thiamine: Whole cereals, milk, meat.

Riboflavin: Milk, eggs, liver, green vegetables.

Niacin: Milk, lean meat, liver.

Folic acid: Green leaves, liver, whole cereals.

Vitamin B_{12}: Meat, liver, milk.

Ascorbic acid: Oranges, lemons, grapefruit, tomatoes.

Vitamin D: Fish liver oils, milk, eggs, liver.

Vitamin E: Cereal oils, wheat germ oil, lettuce, milk, butter, meat.

Vitamin K: Spinach, cabbage, liver, egg.

What are the possible toxic reactions from vitamins?

For the most part, there appear to be relatively few ill effects from hypervitaminosis or from allergic reactions. The following may occur in children given large quantities of vitamin A for a number of months: hyperirritability, dry skin, sparse hair, swelling over long bones, high plasma A levels, elevated serum alkaline phosphatase, and x-ray evidence of hyperostoses of the long bones. Likewise, hypervitaminosis D may result from huge doses (especially in arthritic patients), giving rise to loss of weight, anorexia, nausea, vomiting, muscular weakness, apathy, hypercalcemia, phosphatemia, bone changes simulating those of osteitis fibrosa cystica, and calcification of cartilage, blood vessels, and organs. Aside from the above, little has been proved concerning the untoward reactions of the vitamins.

Define phosphatase activity.

Phosphatases are enzymes capable of hydrolyzing phosphoric esters. From a clinical standpoint interest is centered particularly upon the phosphatase activity of the blood plasma (or serum)—alkaline phosphatase and acid phosphatase.

The alkaline phosphatase originates almost exclusively in the bones, where it is formed by actively functioning osteoblasts. An increase in alkaline phosphatase activity is of clinical value in study of patients with diseases of two systems: (1) Skeletal, in which it implies an inadequate mineralization, or, if there has been an injury with attempts at active repair, it implies an adequate bone matrix. Hence, there is an increase in osteomalacia, in which osteoid formation is normal, but not in osteoporosis, which is due to defective osteoid formation. (2) The liver and biliary tract, in which serum phosphatase activity is increased in jaundice due to mechanical obstruction of the bile ducts, hepatocellular jaundice, portal cirrhosis (with levels varying from normal to abnormal) and other forms of focal and diffuse liver disease (abscess, echinococcus cyst, sarcoidosis, etc.). The exact mechanism underlying these changes is not settled.

The acid phosphate of normal plasma originates mainly in the liver and spleen, but, in a large proportion of cases of prostatic cancer, the malignant cells form large amounts of this enzyme and, after they have metastasized to extraprostatic tissues, the serum acid phosphatase activity is increased as the enzyme gains access to the blood. Since no other tissue is capable of forming sufficient amounts of this enzyme to raise its concentration to high levels in the blood plasma, an elevated serum acid phosphatase may be regarded as strong evidence of prostatic carcinoma with metastases. Similarly, it aids in the selection of cases suitable for specific therapy (castration or estrogen administration).

What gland represents the hormone-regulating center of most of the other endocrine glands?

The anterior part of the pituitary gland, which exerts its influence on other glands by means of "tropic" hormones, in response to which these "target" glands in turn produce "tissue affecting" hormones. Since the anterior pituitary is connected by neurohumoral pathways via the hypothalamus with the central nervous system, the hormonal system of the body is to some extent subject to nervous control.

Discuss the role of hormone activity in the adaptation syndrome.

The stimulus arising from local tissue damage by an infection, a burn, an operation, undue exposure to heat or cold, etc., acts upon the central nervous system, which, in turn, causes release from the anterior pituitary gland of adrenocorticotropic hormone. This hormone in turn stimulates the adrenal cortex to increase the production of cortisal ("sugar" hormone), which then inhibits the anabolism of protoplasm in the nondamaged parts of the body tissues. Thus, the damage site is flooded with materials for tissue repair.

Why do fat children sometimes develop slowly?

Fat children are sometimes slow in passing through puberty, not because of any endocrine abnormality—Fröhlich's syndrome or dystrophia adiposa genitalis—but because the gonadal hormones, which are very soluble in fat, are taken up and stored in the excess body fat as fast as they are produced. With weight reduction, the stored hormones are released, bringing about an accelerated rate of development. Thus, most obese children are best treated with dietary measures rather than hormone administration.

Discuss iodine metabolism and thyroid hormone.

The thyroid gland contains an iodized protein "thyroglobulin," which represents the "storage form" of thyroxine, the thyroid hormone, and, in accordance with demand, probably under stimulation by thyrotropic hormone (TSH) of the pituitary, the thyroglobulin in the gland undergoes hydrolysis with release of thyroxine. Under certain conditions, this mechanism may be altered, affecting the formation of thyroid hormone, namely: (1) A deficiency in iodine leads to a deficient synthesis of thyroid hormone and compensatory hyperplasia of the thyroid gland (goiter). Conversely, when iodine is given to patients with hyperthyroidism, it is followed by regressive changes in the gland and a diminished output of hormone. (2) The administration of thyroxine results in a diminished formation of hormone. (3) Certain antithyroid agents, thiouracil, sulfonamides, etc., inhibit synthesis of thyroid hormone, apparently by interfering with the oxidation of necessary inorganic iodide. (4) Administration of thiocyanate results in enlargement of the thyroid and decreased synthesis of thyroid hormone (if blood iodide concentration is low).

Discuss the action of the parathyroid hormone in the metabolism of calcium and phosphorus.

The parathyroid hormone decreases renal tubular reabsorption of inorganic phosphate from the glomerular filtrate. Excessive amounts of the hormone result in excessive loss of phosphate in the urine and a fall in plasma concentration. It accelerates mobilization of calcium from the bones, with resulting increased calcium excretion in urine, increased calcium plasma concentration, and skeletal demineralization.

Outline the main functions of the adrenocorticotropic hormone and adrenocortical steroids.

Although the exact mechanism of action of the adrenocortical secretions is not fully understood, it seems apparent that their principal function is to maintain homeostasis by regulating the volume and composition of body fluids. Under conditions of stress, the activity of the adrenal cortex is greatly increased by the action of the adrenocorticotropic hormone. Since the immediate site of action of the adrenocorticotropic homone is on the adrenal cortex and its ultimate effects result from the secretion of adrenocortical steroids, it seems desirable to discuss the adrenocorticotropic hormone (ACTH, corticotropin) and steroids of the adrenal cortex and their synthetic derivatives together. The adrenocortical steroids are classified as: (1) glucocorticoids, affecting mainly sugar and protein metabolism (cortisone, hydrocortisone, etc.); (2) mineralocorticoids, affecting mainly electrolyte and water metabolism (desoxycorticosterone, aldosterone, and 9α-fluorohydrocortisone); (3) androgenic corticoids (adrenosterone).

For the most part, the physiological effects of cortisone, hydrocortisone, etc. are the same, although quantitative differences exist.

(*1*) *Water and Electrolyte Balance:* Prolonged high dosage of adrenocortical steroids results in edema, hypochloremia, hypokalemia, low-potassium syndrome, and metabolic alkalosis, which are due to salt retention and postassium diuresis. Prednisone and prednisolone, which are three to five times as potent as their parent substance, do not in low doses produce salt retention or excessive potassium excretion.

(*2*) *Carbohydrate, Protein and Lipid Metabolism:* The administration of adrenal steroids causes an increased gluconeogenesis from protein and possibly fat, with a sparing of carbohydrate utilization by those tissues that require insulin. Thus, normal subjects may show a fasting hyperglycemia and glycosuria, and a diminished tolerance to insulin. Diabetics usually require additional quantities of insulin for adequate control while receiving steroid therapy.

(*3*) *Androgenic Function:* These steroids exert an androgenic action that produces signs of excessive male-hormonal activity in males and masculinization in females. Likewise, the adrenal androgens possess a protein-anabolic effect, demonstrated in the rapid growth rate of the prepubertal child with the adrenogenital syndrome.

(*4*) *Regulation of Hematopoiesis and Tissue Reactivity:* Administration of ACTH and adrenocortical steroids to patients with normal adrenal functional capacity produces a striking reduction in the number of circulating eosinophils due to an increased peripheral destruction, a lymphopenia due to increased lysis of both fixed and circulating lymphocytes, a neutrophilia, and a tendency to polycythemia. Both ACTH and the adrenocortical steroids greatly inhibit the reactivity of mesenchymal tissues to injury, irritants, and foreign proteins (including microorganisms). As a result of this inhibiting effect on both fixed and mobile cellular defenses, inflammation is reduced, but resistance to injury and infection may be seriously impaired.

(*5*) *Effects on the Gastrointestinal Tract:* The adrenocortical steroids cause an increased secretion of hydrochloric acid and pepsin by the stomach and also of the pancreatic enzymes. In addition, these steroids appear to facilitate the secretion of bile and increase the absorption of fat from the intestinal tract.

(*6*) *Effects on the Musculoskeletal System:* Muscular weakness may occur as a result of potassium depletion in patients receiving these steroids. With prolonged high dosages, these hormones may cause osteoporosis or may intensify that previously existing, so that pathological fractures occasionally occur. This is a result of increased nitrogen loss and increased output of calcium and phosphorus.

(*7*) *Effects on the Cardiovascular System:* Elevation of blood pressure rarely accompanies the administration of small doses of steroids, but, in the presence of renal failure and adrenal insufficiency, their ability to increase blood pressure is accentuated.

(*8*) *Effects on the Central Nervous*

System: Psychological changes produced by administration of these hormones may include exaggerated sense of well-being, euphoria, and increased appetite, as well as a variety of psychotic reactions, such as depressions or frank psychoses. Abnormal electroencephalograms are also found in patients receiving these steroids. Brain excitability is increased and convulsive seizures may occur, especially in children.

Characterize the changes in maternal hormone production during pregnancy.

Estrogen and *progesterone* production are the task of the ovarian corpus luteum during the early weeks of pregnancy. Once pregnancy is established, the maintenance and growth of the corpus luteum are accomplished by the luteotropic hormone, *chorionic gonadotropin,* which is synthesized by the cytotrophoblasts of the growing ovum. This placental hormone is detectable in the maternal blood as early as the second week of embryonal life. Its concentration in the maternal blood is only 5 to 30 I.U. per ml. during the first 6 weeks. Then the level rises rapidly, reaching a peak of about 600 I.U. per ml. between the eighth and tenth week. Thereafter, the concentration falls rather abruptly to early pregnancy levels and remains there for the rest of the gestation. Meanwhile, the amounts of circulating estrogens and progesterone begin to rise. They climb steadily from early pregnancy to shortly before the onset of labor, when they fall abruptly. After the sixth week of pregnancy, almost all estrogenic production is accomplished by the syncytiotrophoblasts of the placental chorion. Although the same cells manufacture progesterone, the ovary shares appreciably in production of this hormone for most of the first trimester. Indeed, it continues to produce some progesterone for several more months. Enough progesterone is being manufactured by the placenta by the end of the sixth week, however, that in some (but not all) cases, the ovarian corpus luteum can be excised without causing abortion. Estrogen and progesterone combine to effect the tubal activity that transports the fertilized ovum. Together they increase the uterine blood supply and bring about the breast changes of pregnancy. Estrogens stimulate ductile proliferation and progesterone, growth of the glandular elements. The estrogens also promote myometrial development and uterine contractility throughout pregnancy. At the same time, however, they inhibit uterine contractility engendered by uterine distention. Progesterone is responsible for the tubal and uterine secretions that nourish the very young fertilized egg. It initiates the postovulatory elevation in basal temperature which, with pregnancy, continues for most of the first trimester. It also plays a role in protein catabolism and in sodium metabolism. Most important, however, is its essential role in maintaining the pregnancy. Progesterone inhibits excessive and dangerous myometrial activity throughout pregnancy. Its acute withdrawal shortly before the onset of labor is probably the most important factor in initiating labor. Androgenic activity is mildly decreased during pregnancy. The urinary excretion of both *androsterone* and *etiocholanolone* gradually diminishes as the gestation grows. The lowest levels occur near or during the last trimester. Thereafter, they gradually return toward normal. Production of the *adrenal hormones* has been thought to increase, but recent work tends to refute this. It is true that the blood and urinary levels of the steroids and their metabolic products increase. Evidence suggests, however, that this is due to alterations in metabolism and excretion rather than to an increase in production. Be that as it may, the urinary glucosteroids rise to a minor crest at about the eighth week of pregnancy, then fall away only to rise to a much higher level at about the thirtieth week. From this gradual peak, they slowly decline again. The urinary 17-ketosteroids and plasma 17-hydroxycorticosteroids increase gradually from early pregnancy to term, and the aldosterone content of the urine also rises. The latter, after a rapid increase during the first two trimesters, falls slowly in the last trimester. The meaning of these changes is uncertain.

The activities of the pituitary hormones during pregnancy are also incompletely understood. It is known that the gland increases in size. *Prolactin* is certainly increased both during pregnancy and lactation. During the first trimester of pregnancy, it may have a luteotropic action. After delivery, it initiates lactation. Thyrotropin is increased and the posterior-lobe hormones also increase during pregnancy. Although *oxytocin* is normally a strong stimulus to uterine contractility, the uterine muscle remains refractory to it during pregnancy until the last trimester. As term approaches, responsiveness of the myometrium returns and the muscle finally becomes extremely sensitive to the presence of oxytocin. This hormone also has a milk ejection or "let down" effect, which is important to lactation. The other posterior pituitary hormone, *vasopressin*, increases during pregnancy and lactation. Its primary action is antidiuretic; its diuretic action is neutralized, however, during the second half of pregnancy.

The thyroid gland enlarges diffusely during pregnancy and its activity increases. How its many regulatory actions are influenced by the gestation is not completely worked out. Increased oxygen utilization and metabolism are reflected by basal metabolic rates that may reach into the twenties. Increased hormonal synthesis and increased body utilization are reflected by rises in uptake of radioactive iodine and by increases in PBI levels. These values may be twice as high during pregnancy as compared to the nonpregnant state.

Discuss the physiology of lactation.

During pregnancy, estrogenic hormone stimulates additional development of the ductal system of the breast and, with progesterone, exerts a similar effect on the acinar tissue. After delivery, two hormones from the anterior lobe of the pituitary, *prolactin* and *galactin*, cause the secretion of milk. The presence of adrenal cortical hormone is also necessary. It is believed that the pituitary hormones are released by the withdrawal of the ovarian hormones and, probably, the disappearance of the anterior-pituitary–like hormone produced by the placenta.

Colostrum, which is present in the breast during the latter trimester of pregnancy, is secreted by the breasts during the first two or three days postpartum. It is replaced by milk, after a 24- to 48-hour period of breast engorgement. The reflex (probably through the sympathetic pathways) initiated by suckling is necessary for the maintenance of lactation. Nursing (or pumping) not only delivers the milk from the acini but causes most of the milk to form. That is, most of the milk bursts into the acinar lumen from the rupture of the secreting acinar cells during the first part of the act of nursing.

Discuss briefly the physiology of menstruation.

Menstruation is caused by necrosis of the endometrium. However, the uterine lining is controlled by the ovaries, which in turn are directed by the anterior pituitary.

The menstrual cycle, reduced to its barest physiological essentials, occurs in the following manner. The cycle is initiated by the follicle-stimulating hormone of the anterior lobe of the pituitary. The hormone activates the growth of an ovarian graafian follicle, the granulosa cells of which produce follicular fluid containing follicular or *estrogenic* hormone. The ovarian hormone causes the uterine endometrium to grow (proliferative phase). The luteinizing hormone of the anterior pituitary appears and, together with the follicle-stimulating fraction, causes follicular rupture, or *ovulation*, about fourteen days before the next menstrual period. The collapsed follicle is called a *corpus luteum*. The granulosa cells are altered by the luteinizing pituitary hormone. The resultant lutein cells produce their own secretion, corpus luteum hormone or *progestin*, and continue to form estrogenic hormone. These two ovarian hormones stimulate additional growth of the endometrium and cause secretion of its glands (the secretory or progestational phase). If fertilization does not occur, the life of the corpus luteum is about fourteen days. As it degenerates, the fall in the ovarian hormonal titer lessens the stimulus to endometrial growth. The endometrium shrinks, and a series of vascular and tissue changes develops, causing necrosis of all but the basilar layer. Blood from the arteries and venous sinuses, together with the necrotic endometrial tissue, escapes through the vagina as the menstrual discharge.

What conditions influence the quantity of gonadotropic hormones in the blood and urine?

The quantity of this hormone in the blood and urine is increased in pregnancy, primary hypogonadism, chorionepitheliomas, hydatidiform mole, testicular tumors, menopausal syndrome, and male climacteric. The blood and urine gonadotropins are diminished or absent in panhypopituitarism, pituitary cachexia (Simmonds' disease), chromophobe tumors of the hypophysis, and secondary hypogonadism.

What is the "template theory" of gene transmission?

The weight of recent evidence points toward the fact that the information carried by the genes is coded in the deoxyribonucleic acid (DNA) component of the chromosomes. It is believed that the DNA molecule produces a template, or pattern, of itself, which in turn can produce many copies of the original molecule.

BLOOD AND SPLEEN

Discuss the functions of (1) the circulating red blood cells, (2) white blood cells, (3) the platelets, (4) the fixed cells of the reticuloendothelial system, (5) the reticuloendothelial system, and (6) the plasma cells or lymphocytes in the spleen and lymph nodes.

(1) The primary function of the circulating red cells is to maintain in the circulation the high concentration of hemoglobin essential for the transport of large amounts of oxygen necessary for the respiration of the tissues. (2) The white cells, by virtue of their phagocytic and other properties, assist in arresting invasion of microorganisms or in the repair of tissues. (3) The platelets are concerned in maintaining the integrity of the vascular endothelium and thus preventing the escape of blood from the blood vessels. (4) The fixed cells of the reticuloendothelial system are characterized by their powers of phagocytosis of particulate matter. (5) The reticuloendothelial system is concerned in the conversion of hemoglobin to bilirubin and in the storage of iron. (6) The plasma cells or lymphocytes in the spleen and lymph nodes are involved in the production and delivery of antibodies to the circulating blood.

What is the average normal life span of red blood cells in the circulation and by what methods are they destroyed?

The average normal life span of circulating red cells is 100 to 120 days. There are at least four ways in which the red cell may be destroyed, normally or in hemolytic anemias, namely: (1) mechanical destruction because of the traumatic effect of the motion of the circulation on the red cells; (2) hemolysis of red cells by specific agents in the plasma; (3) osmotic lysis, and (4) phagocytosis of red cells by cells of the reticuloendothelial system.

What is the outstanding defect common to all types of anemia and what mechanisms provide compensation for it?

The decreased capacity of the blood to transport oxygen, for which two important methods provide compensation, namely: the rapidity and volume of the circulation of the blood from the lungs to the tissues and return (increased cardiac output and blood flow velocity) and increase in the percentage of oxygen removal from each unit of blood as it traverses the tissues.

Discuss the various functions of the spleen.

The spleen is an organ in which blood-cell formation, blood-cell sequestration, and blood-cell destruction occur normally as balanced physiological functions. If the spleen becomes involved in an acquired, congenital, or inherited disorder affecting one of these functions, a corresponding atypical clinical syndrome will develop.

Give an important cause of deficient erythropoiesis by the bone marrow.

Nutritional deficiency giving rise to a deficiency of vitamin B_{12}, folic acid, or both folic and ascorbic acids which results mainly in a decreased rate of red-cell production; or a deficiency in iron, or possibly copper, which gives rise to a diminished rate of hemoglobin production.

What is the action of the intrinsic factor?

The action of the intrinsic factor is to enhance the absorption of vitamin B_{12} from the alimentary tract.

Discuss the etiology of hypochromic anemia.

The development of hypochromic anemia depends on the magnitude of the demand for iron created by such conditions as loss of blood, demands of growth, pregnancy, etc., relative to the available stores of iron, the iron content of the food, and the effectiveness of its absorption from the alimentary tract. Since iron is probably not absorbed unless it becomes ionized and reduced to the ferrous state, the insoluble ferric forms present in the food are presumably dissolved in the acid gastric secretions and then reduced by ascorbic acid and other reducing substances of the food. Hence, achlorhydria must be supposed to affect this process adversely.

Why do chronic disturbances of renal function often result in anemia?

The exact basis for decreased red-cell formation in the presence of an elevated nonprotein nitrogen due to chronic disturbances of renal function remains obscure. However, it is said that blood phenols are elevated in this type of anemia and may thus cause injury to the bone marrow. Furthermore, other factors, such as the influence of infection and chronic blood loss, may be involved.

What is the basis of polycythemia vera?

It is probably due to an increased red-cell and hemoglobin production as has been shown with labeled isotopes and not to increased longevity of the red cells.

Discuss the function of monocytes.

The monocytes digest microorganisms containing protein and carbohydrate and can attack bacteria with a fat-containing capsule, such as the tubercle bacillus, and thus play a specific role in immunity to tuberculosis.

What mechanisms are involved in producing leukopenia?

(1) Decreased production by the bone marrow as a result of nutritional deficiency of folic acid or vitamin B_{12}; toxic action, or sensitivity to certain drugs and chemicals (benzol, sulfonamides, thiouracil, chloramphenicol, chlorpromazine, etc.) and as a result of intoxication of leukopoiesis by overwhelming bacterial invasion. (2) Increased loss or destruction of leukocytes as seen in cases of hypersplenism. (3) Redistribution of leukocytes in the vascular channels of certain internal organs, such as the liver,

lung, and spleen. This mechanism is considered to be involved in the leukopenia observed in anaphylactoid shock and in the early stages of the reaction to foreign protein.

What are the hypersplenic clinical syndromes?

The acute or chronic selective sequestration and destruction of red blood cells (congenital or acquired hemolytic icterus), platelets (thrombocytopenic purpura hemorrhagica), granulocytes (primary splenic neutropenia), or any combination of them (including primary congenital or secondary acquired panhematopenia) form the background for the broad, general, physiopathological concept of "hypersplenism." The basic mechanism for the hypersplenic phenomena has been attributed to a "hormone" influence emanating from the spleen and acting to inhibit the delivery of one or more of the essential blood-cell elements arising in the bone marrow. All of the above diseases have been successfully treated by the surgical removal of abnormally functioning splenic tissue.

Outline the role of phagocytosis in the pathogenesis of pneumoconiosis.

Fibrosis of the lung may be caused by several types of body response to injury by bacteria or inorganic matter. Fibrous tissue forms about tubercle bacilli to form the wall of a tubercle, etc. Likewise, it surrounds abscesses due to the deposition of inorganic dust particles to delimit them; it is the lesion of pneumoconiosis. Although each type of dust invokes a particular response (silica, fibrosis; asbestos, nodular necrosis; carbon, lymphatic, and lymph-node changes, etc.), the phagocytes that originate in the walls of the alveolar septa play a primary role in removing all particles deposited in the alveoli. After taking on their load, the phagocytes move to the alveolar ducts; some are rendered harmless by the ciliary action, but many enter the lymphatics and set up a foreign-body response with resulting fibrosis of the small lymphatic radicles or in the larger channels. The extent and rapidity of the formation of fibrous tissue are dependent primarily on the type (exposure to carbon takes much longer than exposure to silica).

Outline the successive steps in the development of agranulocytosis.

Sensitization as a result of previous administration of the drug; granulopoietic shock of the leukopoietic tissue of the bone marrow; granulocytopenia of the circulating blood and tissue; failure of defense against bacteria normally present in such areas as the mouth or rectum; local infection and development of necrosis; generalized infection with chills and fever; and, finally, overwhelming sepsis with death (Dameshek).

By what clinical method is thrombocytopenia detected?

A decreased platelet count; positive tourniquet test, which implies that there is defective contractility of the vessels, apart from a deficiency of platelets; prolonged bleeding time, which represents failure of the platelets to agglutinate or release the vasoconstrictor principle, 5-hydroxytryptamine; and absent or diminished clot retraction, which is the result of deficiency of the platelets to cause the clot to contract.

What factors are concerned with the defective coagulation of blood?

Defective coagulation of blood is the result of deficiencies of one or more of the following reactions: (1) Platelet or plasma factors concerned in the formation of thromboplastin. Platelets are essential for the formation of thromboplastin, whereas plasma thromboplastin deficiencies, as exemplified by hemophilia, represent a hemorrhagic disease and are considered to be due to a lack of thromboplastinogen (antihemophilic globulin AHG), which is responsible for the delayed conversion of prothrombin to thrombin. (2) Prothrombin, or accelerators of the conversion of prothrombin to thrombin, which are concerned with deficiencies of the labile (proaccelerin) and stable (proconvertin) factors and hypoprothrombinemia which is closely related to vitamin K deficiency. (3) Fibrinogen to fibrin, in which reduced plasma fibrinogen results in mechanically ineffective clots. Furthermore, the incoagulable state of the blood of patients suffering with shock due to infections, burns, or transfusion reactions may be the result of fibrinolysis; this phenomenon is caused by the liberation of activators within certain tissues of the body that are capable of activating the profibrinolysin of the blood which contributes to the formation of plasma fibrinolysin.

What factors influence the clinical manifestations of leukemias and related processes?

The clinical manifestations of leukemias and related processes (lymphosarcoma, Hodgkin's disease, aleukemic leukemia) depend upon: (1) the cell type affected, as lymphocytes, monocytes, myelocytes, etc.; (2) the tendency of the process to remain localized to certain organs or to metastasize widely, as lymphosarcoma, or to invade the blood stream profusely, as leukemia or aleukemic (subleukemic) leukemia; (3) the aggressiveness of the process, which is usually correlated with the degree of differentiation of the typical cells and is described as acute, subacute, or chronic.

Discuss certain chemical changes associated with the increased metabolic activities of white cells in leukemia.

There is an increased total nitrogen and uric acid of the blood and the endogenous uric acid elimination is greater than normal. The total plasma proteins are decreased, especially in myelogenous leukemia, and the albumin-globulin ratio may be reversed. However, hyperproteinemia is often noted in multiple myeloma, which is largely due to the increase of various globulins.

Explain the mechanism by which edema and jaundice occur in erythroblastosis fetalis.

Edema is probably the result of endothelial damage and hypoproteinemia. The former is the result of anoxia, which results from the hemolytic anemia, erythroblastemia, and macrocytic anemia. The hypoproteinemia is due to liver damage which is also secondary to the anoxia and is contributed to by intrahepatic changes due to extramedullary erythropoiesis which occurs in the liver.

Jaundice results from the hemolysis of red cells, which is caused by the maternal antibodies passing through to the fetal circulation. It is further contributed to by obstructive jaundice secondary to liver damage.

Define hemoglobinemia.

Hemoglobinemia, or hemoglobin free in the plasma, is a manifestation of severe hemolytic anemias. It occurs when excessive numbers of erythrocytes are destroyed very rapidly as a result of the following factors: bacteria (hemolytic streptococcus, typhoid, clostridia, etc.), protozoa (malaria, blackwater fever, etc.), chemical agents (arsphenamines, phenylhydrazine, sulfonamides, etc.), vegetable poisons (favism, poisonous toadstools, etc.), snake venoms, transfusions with incompatible blood, paroxysmal nocturnal hemoglobinuria (syphilis and cold hemolysins), serum sickness (tetanus), etc. Hemoglobinemia is accompanied by anemia, reticulocytosis, and an increase in serum bilirubin. Excessive amounts of urobilinogen are excreted in the urine and feces.

CIRCULATORY SYSTEM

Give the functions of and describe the normal circulation.

The main functions of the circulation are the distribution of oxygen and other nutrient and essential constituents through the capillaries to the tissues throughout the body, and the elimination of noxious products, mainly through the lungs and kidneys. The peripheral venous blood enters the right atrium through the superior and inferior venae cavae. After diastolic filling, the atrium contracts and almost immediately the ventricle contracts, seven eighths of the blood going from atria to ventricles during diastole. When the right ventricle contracts, the tricuspid valve between the right atrium and ventricle, which had been open, now closes, the pulmonary valve opens, and the blood is sent through the pulmonary artery to the lung capillaries. There carbon dioxide is liberated and oxygen is absorbed. Thus the venous blood becomes arterial. The blood then returns, by way of the pulmonary veins, to the left atrium and passes through the mitral valve into the left ventricle. As the ventricles contract, the mitral valve closes, the aortic valve opens, and the arterial blood leaves the left ventricle through the aorta to enter the systemic circulation.

Name the factors involved in maintaining the pulse pressure.

(1) The pumping action of the heart—cardiac output; (2) the peripheral resistance, i.e., an increased resistance in the arteriole; (3) the amount of blood in the arteries; (4) the viscosity of the blood; and (5) the elasticity of the arterial walls.

What influences the flow of blood to the heart through the veins?

(1) The energy imparted to the blood by its ejection from the left ventricle; (2) thoracic pressure, including effective venous pressure as well as compression of abdominal structures and increased pressure in the inferior vena cava with the descent of the diaphragm in inspiration; (3) venopressor mechanisms—valves in the veins, muscular structures surrounding veins, etc.; and, (4) nervous control, which maintains venous and capillary tone, etc.

What nerves control the action of the heart?

(1) The intrinsic mechanism, consisting of ganglia in the heart wall; (2) the extrinsic mechanism, consisting of cardio-inhibitory and cardioaccelerator fibers. The cardio-inhibitory center is situated in the nucleus of the spinal accessory nerve, and the impulses are conveyed through fibers of that nerve to the vagus, which is the great cardio-inhibitory nerve. The cardioaccelerator center is hypothetical and is probably situated in the medulla. The fibers pass out through the first five dorsal nerves (particularly the second and third) to the sympathetic ganglia, from which fibers pass to the heart as the cardiac sympathetic nerves. The vagus also contains some accelerator fibers.

In what manner is the heart beat influenced by the vagus nerve?

Stimulation of the vagus nerve causes slowing of the heart. If the stimulation is continued, the heart beat may be accelerated, because of either direct stimulation of the accelerator fibers in the vagus or the intervention of the accelerator mechanism. The latter is probably induced by both nervous impulse and hormonal influences (epinephrine and norepinephrine).

What is the carotid sinus and what is its importance?

It is a dilatation of the common carotid artery normally present at the bifurcation of the external and internal carotids. It is important because the arterial wall at this point contains sensory endings of afferent cardiac nerves whose function is similar to that of the aortic nerves. The carotid-sinus reflex is a stimulation of the carotid sinus by any act that increases blood pressure, such as holding the breath, choking, or vomiting, or external pressure. This stimulates the vagus reflexly and causes slowing of the heart and, by stimulating the vasodilator fibers, a fall in blood pressure.

What is the myogenic theory of the heart's activity?

The view that the heart muscle fibers possess in themselves the power of originating and maintaining the contraction of the heart, as opposed to the neurogenic theory, according to which the heart contracts only in response to stimulation by the central nervous system.

Define the myogenic functions of heart muscle and state in what portion of the heart each is most active.

(*1*) *Stimulus Production:* This is most active wherever there are remains of the sinus venosus (primitive cardiac tissue), namely, at the orifices of the venae cavae, especially the superior cava, and at a point near the opening of the coronary sinus, in the groove between the left atrium and the left ventricle. Normally, the stimulus originates at the orifice of the superior cava, at a point called the sinoatrial node, and the rhythm is spoken of as a normal or sinus rhythm.

(*2*) *Excitability:* The property of responding to stimuli, possessed by all portions of the myocardium. The contraction is always the maximum contraction of which the muscle fibers are capable at the time, irrespective of the intensity of the stimulus. Increased excitability may be inferred from increased frequency, and, sometimes from the occurrence of extrasystoles; conversely, diminished excitability may show itself in bradycardia and intermittence.

(*3*) *Conductivity:* That function of the fibers of the heart muscle which conveys the stimulus from fiber to fiber. It is studied by observing the time between atrial systole and ventricular contraction, the a-c interval in the phlebogram. Conductivity is most marked in the bundle of His or A-V bundle, which transmits the stimulus from atrium to ventricle.

(*4*) *Contractility:* The power of contracting in response to a stimulus, possessed by the myocardium in common with all other muscle tissue. It resides chiefly in the massive ventricular walls.

(*5*) *Tonicity:* That function of the myocardium which keeps the heart during diastole in a state of moderate contraction. Depression of this function results in dilatation of the heart and of the atrioventricular orifices (relative insufficiency). It is most marked in the muscular rings or sphincters surrounding the valve orifices.

What factors influence the intensity of the first heart sound?

In general, heart sounds are louder in the young than in the old, in the thin than the fat, and in individuals with normal lungs (in emphysema the sounds are markedly reduced). The chief factors that influence the intensity of the first sound are the position of the atrioventricular valves at the onset of systole (depending on P-R interval), the rate of rise of ventricular pressure (hyperthyroidism, beriberi, anemia, exercise, etc.), the presence or absence of structural disease of the mitral valve, and the amount of tissue between the heart and the surface.

Discuss the influence of abnormal heart rates on coronary blood flow.

In general, the flow in coronary vessels depends on the aortic blood pressure and the state of the coronary vessels with the maximum flow usually occurring during diastole and varying in proportion to the heart rate. With abnormal heart rates, such as tachycardia, the coronary flow is decreased, largely as a result of the shortened diastolic period and relatively prolonged systole. The resulting cardiac ischemia gives rise to pain, dyspnea, or alterations of the RS-T segments, or T waves. In severe bradycardia the coronary flow is also diminished, but the involved mechanism is not clearly understood.

Define cardiac reserve.

Cardiac reserve is the capacity of the heart to meet the extra demands placed upon it. In conditions that require greater volumes of blood, such as exercise, digestion, excitement, fever, and various abnormal states, the heart meets the demand by increasing its output. This is accomplished by an increase in cardiac rate, increased diastolic filling and systolic emptying of the ventricles, dilatation of the ventricles, and possibly hypertrophy.

Discuss circulation time determination.

Normal arm-to-tongue circulation time is 10 to 18 seconds, after the injection of 3 ml. of 20 per cent sodium dehydrocholate solution (Decholin Sodium), which produces a bitter taste. Calcium salts may also be employed in this test, in that they produce a warm sensation as they arrive in various parts of the body and may be of help when local disease of the cardiovascular system interferes with the flow of blood to one part of the body (Buerger's disease). Normal arm-to-lung circulation time is 4 to 6 seconds after the injection of 0.3 ml. of ether mixed with 2.0 ml. of isotonic sodium chloride solution, which gives its characteristic odor in the patient's nose or mouth. Circulation time is increased in cardiac decompensation, dehydration, polycythemia, and myxedema; it is decreased in hyperthyroidism, anemia, in patients with right-to-left shunts, and after exercise.

Describe the methods of visualizing blood vessels.

(1) *Ophthalmoscope:* The actual blood column with its width, variations in contour, and its tortuosity is seen, as well as secondary changes—hemorrhage, exudation, and papilledema (arteriosclerosis, hypertensive states).

(2) *Microscope:* With an oblique light and a transparent oil, the capillary loops may be seen in the nail fold. Normally, the loops are of uniform size arranged in parallel rows and the blood stream is seen as a smooth column of blood. With increasing age, the loops increase in length and become tortuous and the capillary flow diminishes. Likewise, various diseases affect the architecture of the loops (arteriosclerosis, Raynaud's disease, etc.), as well as the flow.

(3) *Arteriograms.* The intra-arterial injection of opaque material, such as Diodrast, followed by roentgenograms, may give valuable information concerning the caliber of the artery, variations in collateral circulation, etc., as well as demonstrate arteriovenous fistulas. Venography is also employed particularly for visualization of the large veins and the right and left sides of the heart.

(4) *Direct Visualization.* With appropriate instruments, sigmoidoscope, esophagoscope, etc., the blood vessels may be seen directly in various areas of the body—rectum, bladder, etc.

Give two diagnostic techniques used in the differential diagnosis of congenital heart disease.

(1) *Angiocardiography:* This is of great value when the problem concerns cyanosis due to the shunting of venous blood into the arterial system, "right-to-left shunt." Multiple x-rays of the heart are taken with a special camera, following the injection of a contrast medium (Diodrast) into a systemic vein.

(2) *Cardiac Catheterization:* This may be of help in cases of "left-to-right shunt," since the pressures in the various chambers can be measured and samples of blood for gas analysis obtained. A ureteral catheter is passed through a systemic vein into the vena cava, right atrium, right ventricle, and finally the pulmonary artery.

Describe the mechanism of cyanosis in tetralogy of Fallot.

Originally, four essential features were described as producing the cyanosis: pulmonary stenosis, a ventricular septal defect, a right-sided aortic arch, and right ventricular hypertrophy. However, only the first two anomalies are essential for producing the clinical picture, in that the right ventricular pressure rises to exceed that of the left ventricle and shunting from right to left occurs. The right-sided aorta is not a contributory factor and the right ventricular hypertrophy is a consequence of the pulmonary stenosis.

What is the Goldblatt kidney?

The elevation of blood pressure in both essential hypertension and hypertension secondary to renal disease is the result of an increase in the peripheral resistance, i.e., an increased resistance in the arteriole, but the exact mechanism of this is not clearly understood. Experimentally Goldblatt partially constricted the renal artery in animals with a clamp and produced renal ischemia with a subsequent elevation in blood pressure, which simulated essential hypertension in man. Although this procedure produces hypertension, there appear to be no detectable changes in renal function. Likewise, denervation operations do not prevent the hypertension, which rules out a nervous origin. Further studies to help explain this phenomenon have shown that a pressor substance, renin, is present in the venous blood of the ischemic kidney, which is apparently produced in the kidney cortex. Additional experiments have indicated that the activity of renin is dependent upon a substance (renin-activator) contained in blood or plasma which combines with renin to form angiotexsin (angiotonin, hypertensin) which probably has a direct effect upon the small blood vessels.

Discuss the mechanism of pain in peripheral vascular disorders.

In cases of embolism or thrombosis, the pain results from ischemia, acute arterial insufficiency, although in slowly developing complete occlusions pain may not occur, whereas in acute occlusions there is spasm of associated collateral vessels that contributes to the causation of pain in that sympathetic block relieves it. Likewise, in ulceration and gangrene (Buerger's disease) the pain, as well as the necrosis, is due to ischemia of the part. In arteriosclerosis obliterans, the pain is often severe and extensive and often has nocturnal paroxysmal exacerbations and is thought to be due to ischemic neuritis. Intermittent pain, as seen in intermittent claudication, results from an inadequate supply of blood to the contracting muscles. The same mechanism explains the pain associated with severe anemia. In contrast to the above condition, resulting from the effects of ischemia, pain is also observed with the opposite, excessive hyperemia due to abnormal dilatation of structurally normal vessels. The term "erythromelalgia" is applied to this reaction, which occurs without known cause, as well as in certain known diseases (polycythemia, gout, hypertension, etc.).

Give a brief description of the electrocardiograph and explain the physiologic principle on which it is based.

The contracting heart, like every other contracting muscle, generates an electric current, and if this current (electromotive force) is made to pass through a conductor placed in a magnetic field, the conductor will move in certain directions perpendicular to the lines of force of the magnetic field. The direction in which it moves will depend on whether the current passes up or down the conductor. This principle is utilized in the electrocardiograph, which records the minute electric currents generated in the heart muscle and the differences in electrical potential.

The instrument consists of the following parts:

(1) An *electromagnet* with the north and south poles close together forming a magnetic field, within which is

(2) A *string galvanometer* or conductor suspended vertically between the two poles. This is a very fine quartz thread covered with silver or platinum.

(3) An *electric bulb* and *condenser* to illuminate the string.

(4) A *microscope* so arranged as to magnify the movements of the shadow cast by the string (about five hundred times) as it is projected on the slit of

(5) A *camera* in which it is photographed on a moving film.

(6) A *timing device* which interrupts the light at regular fixed intervals to permit accurate measurement of the time relations in the curve obtained.

In addition there is a dry battery that neutralizes body currents other than those produced in the heart, and certain other necessary accessories.

The heart current is led into the apparatus by means of electrodes. There are four recognized so-called *leads:*

Lead I: Right arm to left arm.

Lead II: Right arm to left leg.

Lead III: Left arm to left leg.

Lead IV, or chest leads or precordial leads, terms that may be used interchangeably and are for practical clinical purposes synonymous. When precordial leads are taken, one electrode is placed over the region of the heart and is called the exploring, chest, or precordial electrode and a second electrode is placed at a distance from the heart and is called the indifferent electrode.

What is the electromotive force (EMF)?

The electromotive force is responsible for the P wave and QRS complex and occurs before the auricular and ventricular muscle fibers contract (not as a result of their contraction).

Discuss the features of the electrocardiogram which are most important for its interpretation.

The typical electrocardiogram consists of a series of waves arbitrarily designated as the P wave, the QRS complex, the T wave, and the U wave. The P wave represents the depolarization wave of the auricular musculature, which spreads radially from the sinoauricular (S-A) node to the atrioventricular (A-V) node. Normally, the P wave is a round upward deflection in leads I and II, and may be positive, negative, diphasic, or notched in lead III and in the chest leads. The height of the normal wave does not exceed 2.5 mm. in any limb lead and should be at least 1 mm. high in one of those leads. The width does not normally exceed 0.11 second. The P-R interval is measured from the beginning of the P wave to the beginning of the QRS complex and represents the time required to depolarize the atrial musculature plus the delay in transmission of the impulse through the A-V node to the beginning of ventricular depolarization (upper limit of normal being 0.20 second). The QRS complex is the depolarization complex of the ventricular musculature and consists, usually, of an initial downward deflection, the Q wave, an initial upward deflection, the R wave, the initial downward deflection after the R wave, the S wave. The R wave, which should be at least 5 mm. high in one of the standard leads, is usually less than the S wave in the V_1 position of the chest leads and (as we go from V_1 to V_6) the R wave gradually increases as the S wave decreases, so that in V_4, and V_5, and V_6 positions, the R wave is usually larger than the S wave. The duration normally does not exceed 0.10 second in the limb leads but occasionally may be 0.11 second in the chest leads and is measured from the beginning of the first wave of the complex to the end of the last wave. Marked notching of the QRS is not normal, although minor degrees of notching (slurring) are usually of no significance. The S-T interval is the duration in seconds from the end of the QRS to the beginning of the T wave and represents roughly the depolarized state, or the duration of the excited state of the ventricular musculature or the interval of time between the completion of depolarization and the beginning of repolarization of the ventricular musculature. This segment should not vary in a positive or negative direction from the iso-electric line to exceed 0.5 mm. in any of the limb leads. In the chest leads, upward variations of 2 mm. and depressions of 0.5 mm. are still within the normal range. The Q-T interval is measured in seconds from the beginning of the QRS complex to the end of the T wave and represents the entire time required for depolarization and repolarization of the ventricular musculature. The Q-T interval varies with age, sex, and cardiac rate—the upper limits of normal being 0.40 second. The T wave should be upright in the first and second limb leads and may be upright, iso-electric, or inverted in the third limb lead. It is variable in height and shape, being at least 0.5 mm. high in leads I and II and not over 5 mm. high in any of the three limb leads. In the chest leads, the T wave may be negative in the first two positions but usually by the third position it becomes positive and normally remains positive the rest of the way. The height of the T wave in the chest leads varies from 1 mm. to 10 mm., the average height of the highest T wave being around 5 mm.

Define the terms "blackout" and "red-out" as related to airplane travel.

Airplanes are subject to forces that far exceed man's adaptive capacity; thus he is unable to deal effectively with the suddenly built-up power of gravity impinging upon him when sharp turns, banks, or loops produce abrupt deviation from linear flight at high velocity. A large part of the resulting difficulty comes from circulating incapacity resulting in pooling of blood. "Blackout" and "red-out" are the terms for cerebral anemia and plethora produced by centrifugal and centripetal forces.

What problems are encountered when man ascends to high altitudes in an airplane?

Reduced atmospheric pressure with alterations in concentration of gases, oxygen, and nitrogen is of chief concern; reduced temperature and problems concerned with acceleration, gravity, and motion.

Discuss the pathogenesis of decompression disease (bends, caisson disease, altitude bends, aeroembolism).

Decompression permits the formation and enlargement of nitrogen bubbles in tissues, both intra- and extravascular. Each bubble actually represents a minute traumatic agent which may cause a variety of vascular responses, the reactions varying with the tissue involved and the severity of bubble formation. Stasis from local spasm or systemic shock favors the intravascular development of bubbles, which may terminate decompression sickness fatally.

Differentiate between forward and backward heart failure.

Forward congestive heart failure is characterized by the following order of events: (1) decreased cardiac output, (2) decreased excretion of salt by the kidneys, (3) increased blood volume, (4) edema formation, and (5) elevation of the venous pressure. In backward congestive heart failure, the order of events is: (1) increase in venous pressure, (2) decrease in effective circulating blood volume, and (3) salt retention by the kidney and elevation of the blood volume, both resulting from vasoconstriction.

Give the principal manifestations of left-sided heart failure.

Dyspnea, orthopnea, paroxysmal dyspnea, cough, occasional chest pain, rales, hydrothorax, decrease in vital capacity, increase in the pulmonary circulation time, and rise in the left atrial pulmonary artery and pulmonary venous pressures. These symptoms, signs, and laboratory findings result from engorgement of the pulmonary vascular tree consequent to elevation of the end diastolic pressure in the left ventricle and left atrium.

List the important extracardiac conditions affecting the function of the heart.

(*1*) *Hypertension:* Acute hypertension, as occurs in toxemia of pregnancy and acute glomerulonephritis, may cause a rapid dilatation and failure of the heart. Chronic hypertension gives rise to cardiac hypertrophy, which is the most important cause of congestive heart failure and favors the development of coronary arteriosclerosis, which represents an important factor in the causation of angina pectoris and myocardial infarction.

(2) *Hypotension:* Reduction of coronary blood flow, which occurs in such hypotensive states as hemorrhage and traumatic shock, may interfere with myocardial metabolism and may play an important role in the production of the irreversible stage of shock.

(3) *Anemia:* In patients with severe anemia, an increase in heart rate and an augmentation of stroke volume occur in an attempt to compensate for the diminished oxygen-carrying capacity of the blood. If the anemia persists, cardiac hypertrophy may occur, and, if the output is inadequate to compensate for the reduction of hemoglobin in the heart muscle, hypoxia may develop.

(4) *Thyroid Dysfunction:* In hyperthyroidism, the increase in circulatory rate that results from the increased metabolic demands of the tissues, if of long standing, may lead to cardiac hypertrophy and failure. Likewise, cardiac efficiency is reduced by the onset of atrial fibrillation, which often occurs in cases of hyperthyroidism. In myxedema, the heart may become dilated probably as a result of myocardial weakness, and congestive heart failure sometimes occurs. Likewise, the disturbance of lipid metabolism in chronic hypothyroidism favors the development of coronary atherosclerosis, with resulting symptoms of angina pectoris.

(5) *Pulmonary Disease:* In long-standing pulmonary disorders, such as obstructive emphysema, cystic disease, and diffuse fibrosis of the lungs, pulmonary hypertension often occurs, giving rise to cardiac hypertrophy with eventual failure. Likewise, kyphoscoliosis often terminates in a similar way. Pulmonary embolism may so diminish the flow of blood through the lungs and the left side of the heart as to cause acute dyspnea (acute cor pulmonale).

(6) *Infections:* The work of the heart is increased when the body temperature is elevated, and in patients with pre-existing heart disease an infection may cause the heart to fail. In certain infectious diseases—rheumatic fever, diphtheria, scarlet fever, pneumonia (bacteria or viral)—acute myocardial degeneration may accompany or may follow the infectious process.

(7) *Abnormal Metabolic States:* Heart failure is characteristic of thiamine deficiency; the cardiac output is increased in hypoglycemia and in uremia; the retention of potassium may lead to myocardial weakness, conduction disturbances, and abnormalities of impulse production.

What factors are involved in hypoproteinemia in congestive heart failure?

Increased plasma volume (water), prolonged albuminuria, decreased protein intake, impaired digestion, diminished absorption from the edematous intestinal mucosa and impaired synthesis as a result of hepatic malfunction.

THE RESPIRATORY SYSTEM

What are the functions of the lungs?

(1) Ventilatory, the displacement of air into and out of pulmonary tissues; (2) alveolar, the distribution of inhaled air to perfused alveolar spaces, and the conveyance of oxygen and carbon dioxide between alveolar air and pulmonary capillary blood; (3) vascular, the passage of the entire blood circulation through the pulmonary vascular bed.

List the factors necessary for effective pulmonary ventilation.

(1) Patent airways, to permit sufficient air to be brought in through the upper airway, moved along the trachea into the major bronchi, and then distributed into the myriad alveoli. (2) Elastic and expansile lungs and tracheobronchial tree, to provide amplitude of respiration. (3) Terminal alveolar structures that can be evenly aerated and pro-

vide a large surface of well-perfused capillaries. (4) Adequate musculoskeletal apparatus of chest wall and related structures, so as to move large volumes of air in and out of the lungs rapidly under conditions of maximum stress.

Describe the function of the mucous membrane of the respiratory tract.

(1) The mucus secreted by the glands arrests dust particles and other foreign bodies in the inspired air, and the ciliated epithelial cells keep the lungs clear of accumulations of mucus and the suspended dirt particles. (2) The squamous cells lining the air vesicles, by virtue of their vital activity, play a part in the exchange of respiratory gases.

Discuss the regulation of breathing.

The primary mechanisms of the control of breathing are chemical or nervous in origin. The chief chemical factors in the blood are the tension of carbon dioxide and of oxygen, and the hydrogen-ion concentration. These three stimulate breathing by increasing the hydrogen-ion concentration of the respiratory center, although anoxia exerts its influence largely through the carotid-sinus mechanism. The nervous factors that regulate breathing include reflex influences on the respiratory center, arising in almost any part of the body; those arising in the lungs, the vagal stretch reflexes (Hering-Breuer reflexes), are the most important. Other important reflexes arise in the muscles and joints, and the carotid and aortic bodies contain chemoreceptors that play a definite role in the control of breathing.

Give the mechanism of respiration.

This consists in alternating dilatation and contraction of the thoracic cage; the dilatation is termed *inspiration* and the contraction, *expiration*. The lungs lie wholly passive within the thoracic cavity, and by virtue of their complete elasticity follow every change in the capacity and shape of the thorax. Enlargement of the thorax is effected by certain muscles known as the muscles of inspiration; the diaphragm descends and at the same time is withdrawn from the chest walls; the ribs are elevated and rotated outward. At the end of inspiration the muscles relax and the thorax collapses, expiration being usually a passive process owing to the elasticity of the lungs, the weight of the chest, the tension of the abdominal muscles, and the torsion of the costal cartilages. It is also assisted to some extent by the action of the muscles of expiration. The respiratory movements are controlled by a center in the medulla.

Define the following terms: (1) total lung capacity (pulmonary volumina), (2) maximum breathing capacity (M.B.C.), and (3) the dead space.

(1) The total lung capacity is the total volume of air in the lungs at maximal inspiration, which represents the sum of the inspiratory capacity (the maximal volume of gas that can be inspired from the resting expiratory position) and the functional residual capacity (the volume of gas remaining in the lungs at the end of a resting expiration); or the sum of the vital capacity (the maximal amount of gas which can be expired after a maximum inspiration) and the residual volume (the amount of air remaining in the lung at the end of a maximal expiration). (2) Maximum breathing capacity (M.B.C.) represents the greatest volume of air that can be ventilated by voluntary effort during a given interval. (3) The dead space is the volume of the respiratory passages from nose through bronchioles within which there is no rapid exchange of respiratory gases.

Discuss the role of carbonic anhydrase in the respiratory phase of pulmonary function.

This enzyme is present in red blood cells and is active, both at the tissue level in converting cellular carbon dioxide to carbonic acid and at the capillary level in converting carbonic acid to carbon dioxide and water, and thus accelerates the volume of carbon dioxide crossing the alveolar barrier.

Give a classification of acidosis and alkalosis.

The primary factor in respiratory disturbances of the acid-base balance is that pulmonary ventilation can rapidly change the carbon dioxide pressure of blood, thereby producing an abnormal bicarbonate (or carbon dioxide) content in the presence of a normal buffer base. Since the body regulates both the arterial or alveolar carbon dioxide pressure (pCO_2) and the buffer base of the whole blood, the two conditions are classified as "respiratory" (pCO_2 being the primary disturbance) or "metabolic" (buffer base of the blood being primarily disturbed).

Differentiate respiratory "acidosis" and "alkalosis."

Respiratory "acidosis" (primary carbon dioxide excess) may be defined as a primary increase in pCO_2 and may be encountered in certain types of pulmonary disease, such as severe emphysema, extensive bronchopneumonia, depression of the respiratory center, and convulsive apnea. Respiratory "alkalosis" (primary carbon dioxide deficit) is a primary decrease in pCO_2 and is most commonly seen in the so-called hyperventilation syndrome of anxiety states, but may also occur at high altitudes, and in the presence of encephalitis or hyperthermia.

Since the oxygen percentage of a given sample of air is the same at sea level and at 25,000 feet altitude, why is it necessary to supply extra oxygen at high altitudes?

Two factors are important in maintaining an exchange of oxygen between the alveoli and the blood: (1) the actual oxygen content in volume per cent contained within the alveoli (16.3 vol. per cent); and (2) the partial pressure of oxygen. The partial pressure refers to the total atmospheric pressure multiplied by the per cent concentration of oxygen. The exchange of gases across the alveolar membrane is dependent upon differences in pressure on either side of the membrane (i.e., venous blood has a relatively low oxygen tension, or partial pressure, and will take up oxygen from the alveoli. The reverse is true of CO_2). Therefore, as one approaches high altitudes, the partial pressure or oxygen tension in the alveoli falls as the atmospheric pressure falls, and a point is soon reached at which the hemoglobin can no longer become fully saturated with oxygen. This critical level of partial pressure varies from individual to individual and with the speed of ascent. An altitude of 10,000 feet is considered the point at which the partial pressure begins to drop to critical levels; 23,000 to 25,000 feet is about the limit which acclimated individuals can tolerate.

Define and give examples of four types of anoxia.

Anoxia refers to a lack of oxygen at the tissue level and may be divided into four fundamental types.

(*1*) *Anoxemic Anoxia:* In this the volume and tension of oxygen in the arterial blood are reduced. This type is one of the principal concerns of life at high altitudes and is the main type of anoxia due to pulmonary disease (pneumonia, pulmonary edema, emphysema, etc.).

(*2*) *Anemic Anoxia:* This is due to decreased functioning hemoglobin as a result of anemia or to a decreased oxygen-carrying capacity of hemoglobin because of its change to methemoglobin, or carbon monoxide hemoglobin (carboxyhemoglobin).

(*3*) *Stagnant Anoxia:* This is due to disturbances in circulation, as when the capillary flow is inadequate to supply the tissue needs for oxygen, although the arterial oxygen is normal as it leaves the heart, as in peripheral collapse with shock.

(*4*) *Histotoxic Anoxia:* This is a result of interference with cellular respiration by inactivation or impairment of the respiratory enzyme system. The best example of this type of anoxia is cyanide poisoning.

In which disease is orthopnea usually present?

Congestive heart failure. The erect posture serves to reduce venous pressure and pulmonary congestion and thus diminish the resistance to breathing. In this manner the result is similar to that of phlebotomy or digitalization.

Differentiate between exertional breathlessness and exertional cardiac dyspnea.

Although dyspnea is most frequently seen in those persons whose breathing reserve (B.R.) is low, the term means difficult or painful breathing and is therefore a subjective state, the recognition of which depends upon what the patient says. Hence, the breathlessness experienced by a runner may objectively simulate that observed in a patient with reduced cardiac reserve after mild exertion—rapid, deep breathing with little pause between expiration and inspiration. In the cardiac, oxygen demand and increase in lactic acid are present to the same degree after much less exercise; the pulmonary vascular congestion gives rise to inspiratory excitation; there may be sufficient pulmonary edema and bronchospasm to make breathing difficult; and also the cardiac patient may experience a feeling unknown to the runner—apprehension. Thus, exertional breathlessness and exertional cardiac dyspnea are quite different, but the neurohumoral elements of the two states are similar.

Discuss the mechanism and clinical significance of cough.

Cough is a reflex mechanism initiated by irritation of the nerve endings in the tracheal and bronchial epithelium and may be initiated by extrinsic causes (gases, particulate matter, etc.) but most frequently occurs from accumulated bronchial secretion (mucus, or mucopurulent material). Various sets of muscles participate: those that close the glottis, those that hold the abdominal wall rigid, the diaphragm, the levator and depressor muscles of the ribs, and the bronchial constrictors. Cough is a very common and important symptom and may be beneficial or harmful. At times it removes particulate matter, infected secretions, or viscid mucus that plugs the bronchioles. In such circumstances, suppression with drugs may defeat its purpose. On the other hand, the propulsive action of cough may carry acute infection (pneumonia) from one area of the lung to another; or, in chronic bronchitis or bronchiectasis, the intrathoracic pressure increases during the act of coughing with dilatation of the alveoli resulting in loss of lung elasticity, and emphysema is thus initiated.

What part in the temperature control of the body do the skin and its appendages play?

Approximately 97 per cent of the heat loss from the body is dependent upon the skin. This is brought about by the physical process of radiation, convection, and conduction of heat from the body to the surrounding atmosphere; perspiration loss through the skin; and vapor in the expired air. Perspiration under normal circumstances at moderate temperature is *insensible,* that is, it evaporates as rapidly as it is formed. Insensible perspiration includes both water loss through the skin in this manner and water vapor in the expired air. Moisture is lost directly from the skin capillaries through the skin. In this manner individuals born without sweat glands may lose considerable heat. The evaporation of sweat forms an emergency measure for heat loss when the surrounding atmosphere, temperature and humidity, or muscular work demand more heat loss than is possible through the above mechanisms.

What tests are commonly employed in measuring pulmonary function?

Pulmonary function is determined by measurements of gases in the arterial blood and by measurements of ventilatory capacity. (1) Arterial blood for carbon dioxide content, pH, and oxygen saturation and capacity. Blood sampling at rest and after the standard exercise. (2) Lung volumes, especially vital capacity and residual air. (3) Maximum breathing capacity (M.B.C.) and graphic registration of breathing. (4) Pulmonary ventilation and oxygen consumption. In patients in whom cardiopulmonary surgical procedures are contemplated, special tests are of value, namely: (5) cardiac catheterization, for cardiac output, and pulmonary arterial and right heart pressure; (6) bronchospirometry to measure the performance of each lung separately; and (7) intraesophageal pressures and ventilatory flow rates, to define effort of breathing.

THE DIGESTIVE SYSTEM

State the composition and mechanical functions of the saliva. What relation does the saliva bear to the sense of taste?

Organic constituents: mucin, an albuminous substance, and ptyalin.

Inorganic constituents: sodium chloride, potassium chloride, potassium sulfate, alkaline and earthy phosphates, and ferric phosphate.

The saliva dissolves articles of food soluble in water; moistens such as are ingested in the dry state, assists in the formation of the bolus, and facilitates deglutition by lubricating it with mucus.

In order that a substance may make a gustatory impression, it must be soluble in the saliva; insoluble substances have no taste.

Describe the stages of deglutition.

Buccal Stage: The mouth is closed and the jaws are pressed together by the muscles of mastication. Successive parts of the tongue, from the tip to the back, are pressed against the hard palate, forcing the bolus of food into the pharynx.

Pharyngeal Stage: Return of the bolus to the mouth is prevented by the contraction of the palatoglossus, which brings the anterior palatine arches in contact with each other, and of the styloglossus, which raises the back (base) of the tongue. The larynx is pulled upward and forward, and the glottis closed by approximation of the vocal cords (assisted possibly by the epiglottis). The soft palate is raised by the levator palati, the nasopharyngeal cavity is closed, and the bolus forced into the esophagus by the successive contraction of the three constrictor muscles of the pharynx.

Esophageal Stage: The food is forced downward into the stomach by the peristaltic contraction of the esophageal muscles. Liquids are forced through the pharynx and esophagus by the vigorous contraction of the mylohyoid muscles. The first stage is voluntary, the second and third stages are reflex in character.

What is the etiology of heartburn?

Apparently, heartburn is due to an increased tension in the wall of the lower esophagus and may be produced by the rapid introduction of large quantities of fluid into this area and by local stimulation of the mucosa lining the cardiac end of the stomach.

From the standpoint of gastric acidity, give three main types of abnormal response.

(*1*) *Hyperacidity* (*Hypersecretion*): This is most commonly observed in patients with gastric neurosis, duodenal ulcer, cholecystitis, and in normals who use tobacco to excess; it is due to the secretion of an abnormally large volume of gastric juice, failure of the volume of secretion to diminish during the second hour, and delayed gastric evacuation.

(*2*) *Hypoacidity* (*Hyposecretion*): This is seen in patients with carcinoma of stomach, chronic gastritis, gastric ulcers, chronic debilitating diseases, hyperthyroidism, and in a high percentage of pregnant females.

(*3*) *Achlorhydria:* Absence of free HCl in freshly secreted gastric juice after histamine stimulation is found in approximately 25 per cent of people without gastric disease over the age of 60 years, in pernicious anemia, gastric carcinoma, chronic gastritis, etc. Achlorhydria in the presence of a gastric ulcer denotes carcinoma of the stomach until proved otherwise.

Give the three phases of gastric secretion.

(1) Psychic (or cephalic) phase, due to a nervous mechanism (vagal), as a result of pleasurable sensations (thought, sight, smell, and taste of palatable food). Inhibition of secretion may result from worry, anxiety, and the sight or smell of disagreeable food. (2) Gastric phase, resulting from chemical stimulation of the gastric mucosa of the pyloric antrum which causes a release of gastrin, which in turn is transmitted by the blood stream and acts as a gastric secretagogue. (3) Intestinal phase probably instigated by hormones absorbed from the intestinal mucosa.

What is the action of fat upon the gastric glands?

In the presence of fat, the gastric and intestinal mucosa secretes *enterogastrone*, which decreases both secretion and gastric motility.

Describe the physiology of vomiting.

The vomiting center is situated in the medulla oblongata. The act may be excited by irritation of the centripetal nerves of the palate, tongue, pharynx, or stomach (glossopharyngeal and vagus nerves); reflexly by irritation of the uterus in pregnancy, the intestines (peritonitis), or genitourinary tract; by the sight, smell, or taste of repulsive objects or by repulsive conceptions; and, finally, by direct stimulation of the vomiting center (apomorphine).

During the act of vomiting the walls of the stomach contract, while the cardia is held open by contraction of the longitudinal fibers. Ejection of the contents is assisted by forcible contraction of the abdominal muscles (except in children).

Discuss the pathogenesis of peptic ulcer.

The failure of the mucosa to withstand the destructive action of acid gastric juice, as a result of diminution of cellular resistance or a loss of cellular protection from insufficient secretion of mucus or excessive acid secretion, or a combination of these. The vulnerability of the gastric mucosa to injury is significantly increased by the central nervous system, which may produce hyperemia, hypermotility, and hypersecretion.

Describe the peristaltic movement of the stomach and intestines. What purpose does this movement serve?

The vermicular movement or *peristalsis* of the stomach and intestines is a periodically recurring, progressive contraction of the walls, beginning (in the stomach) at the fundus and ending at the pylorus, attended by the rhythmical opening and closing of the pylorus. Each peristaltic wave lasts 20 seconds and is separated from the succeeding one by an interval of 15 to 20 seconds. Its object is to force the gastric and intestinal contents onward toward the anus. Pendulum-like movements also take place, moving the contents first in one direction and then in the other. Peristalsis is most marked in the small intestine.

Discuss the factors influencing the amount of fat in feces.

Fat is normally present in the feces in three forms, soap fat (combined or fatty acids), free fatty acids, and neutral fat. The relative proportion of each is dependent somewhat upon the efficiency of fat digestion and absorption. Thus, fecal fat may consist of unabsorbed fat and/or fat that has been excreted into the bowel. Fecal fat is increased in cases of severe diarrhea as a result of increased rapidity of passage of food through the bowel, with consequent impairment of absorption; in chronic pancreatitis in which a diminution in the amount of pancreatic lipase in the intestine results in impaired fat digestion; in obstruction of the common bile duct in which condition a disturbance of fat absorption is due to the absence of bile salts in the intestine; in diseases involving the mesenteric lymph nodes (tuberculosis, Hodgkin's disease, leukemia, etc.) which interfere with absorption of fat by obstructing the intestinal lymphatic drainage, etc.

What factors influence the concentration of glucose in the blood?

(1) The rate of entrance of glucose into the blood, which is dependent upon (*a*) hepatic glycogenesis and glycogenolysis, which factor is influenced by blood glucose concentration, insulin, epinephrine, thyroxine, and muscular activity; (*b*) amino acids (gluconeogenesis, in liver); and (*c*) glucose absorption from intestines. (2) The rate of removal of glucose from the blood, which is dependent upon (*a*) blood concentration of glucose, (*b*) insulin, and (*c*) adrenocortical and pituitary hormones.

What is the innervation of the gastric glands? What is the result of stimulation of the nerves?

The gastric glands are supplied with sympathetic fibers from the splanchnic nerves and with parasympathetic fibers from the vagus. Stimulation of the vagus results in the secretion of gastric juice high in peptic power and strongly acid. Stimulation of the sympathetic fibers produces an alkaline, mucinous juice arising directly from the pyloric glands. This secretion is not abolished by atropine but is abolished by ergotamine.

Name the centers and the nerves which regulate intestinal peristalsis and describe their action.

The automatic center resides in the myenteric plexus (Auerbach's plexus) which lies embedded in the muscular coat. Special nerve plexuses, containing ganglia, are found upon the blood vessels and lymph vessels of the intestinal walls. The nerves are the *vagus* and the greater and lesser *splanchnic nerves*. The vagus increases peristalsis and also contains some inhibitomotor fibers. The splanchnic is the inhibitory nerve of the intestinal movements; it also contains the nerves of sensation.

Describe the function of the ileocecal valve.

The ileocecal valve consists of two semicircular folds of mucous membrane containing circular fibers. When the cecum is distended, the valve closes and thus prevents the regurgitation of chyle into the small intestine.

Describe the process of absorption by (1) the blood vessels, and (2) the lymphatics.

(1) Water, alcohol, salts, carbohydrates, and proteins enter the capillary blood vessels and are carried by the *portal vein* to the liver, whence they reach the general circulation through the *hepatic vein.* (2) Fats and fatty acids are taken up by the lacteals and carried to the *receptaculum chyli,* from which they are discharged into the thoracic duct and enter the left subclavian vein.

Describe the structure of an intestinal villus and show how it is adapted for absorption.

A villus is a projection of all the tissues that enter into the composition of the intestinal mucous membrane. It is covered by a single layer of columnar epithelium, with intervening isolated *goblet cells.* Protoplasmic processes resembling cilia extend into the lumen of the intestine like pseudopods, which seize the finely granular fat (*chyle*) and draw it into the cell body. The villus is provided with capillary blood vessels and an axial or central chyle vessel, the *lacteal,* surrounded by adenoid tissue.

What digestive changes take place (1) in the small intestine, and (2) the large intestine?

(*1*) *Small Intestine:* Proteins that have been acted upon by the gastric juice and the albumoses are converted into peptones; fats are split up and emulsified by the action of the bile and of the trypsin in the pancreatic juice. Undigested starch is changed to maltose, which in turn is changed into dextrose by the amylopsin of the pancreatic juice. The succus entericus probably contains an amylolytic inverting enzyme which, however, has little digestive power. Its chief function is to keep the intestinal contents in solution.

(2) *Large Intestine:* Microbial digestion is carried on in the lower part of the small and in the large intestine, resulting in the formation of putrefactive products: carbon dioxide, methane, hydrogen sulfide, hydrogen, phenol, indole and skatole valerianic acid, leucine, and tyrosine. There is but little digestion by organized enzymes in the large intestine; the intestinal contents move slowly, however, and considerable absorption takes place. The large bowel is essentially a "store house" that absorbs water. Although the formation of putrefactive products is unquestioned, their absorption and/or role in producing or enhancing disease is still under question.

What effects result from delayed and depressed intestinal absorption?

Such intestinal disturbances as these are seen in tropical sprue, celiac disease, and idiopathic steatorrhea and give rise to (1) caloric loss from a poor appetite, (2) increased bacterial growth that may interfere with vitamin utilization and synthesis, and (3) modification of intestinal contents as a result of more extensive decomposition of the various foodstuffs by the action of bacteria and enzymes.

What main systems comprise the liver?

Blood vessels, parenchyma, and biliary channels supported by a connective framework, the stroma.

What is accomplished physiologically by the portal circulation?

The great bulk of the products of digestion (proteins, carbohydrates, alcohol, water, and salts) are carried to the liver by the portal vein.

Explain why amebic abscess appears to be more frequent in the right rather than in the left lobe of the liver.

Apparently, portal blood, which represents three fourths of the blood reaching the liver, is not homogeneously mixed, but is channeled, with blood from the splenic, gastric, and inferior mesenteric veins, and carried principally to the left lobe of the liver; whereas blood from the superior mesenteric vein, which transports blood from the right colon (the favorite habitat of these parasites), is carried to the right lobe of the liver.

Outline the main functions of the liver.

(1) *Carbohydrate Metabolism:* The liver plays a part in all phases of carbohydrate metabolism.

(2) *Protein Metabolism:* Its function is the deamination and transamination of amino acids, urea formation, and the formation of certain plasma proteins (albumen, fibrinogen, prothrombin, and globulins).

(3) *Lipid Metabolism:* The action of bile salts on the absorption of fats from the intestines and the metabolism of phospholipids, cholesterol, and neutral fats.

(4) *Vitamin Metabolism:* Absorption of fat-soluble vitamins by the bile salts (liver disease may interfere with the proper metabolism of the water-soluble vitamins).

(5) *Pigment Metabolism:* Bilirubin is removed from the blood stream by hepatic cells and excreted in the bile.

(6) *Inactivation and Detoxification:* The liver inactivates a large number of endogenous and exogenous substances, including bacterial toxins, hormones produced by other glands, and noxious agents absorbed from the gastrointestinal tract; detoxifying processes are concerned with the conjugation and elimination of certain substances by the liver. The ability of the liver to eliminate certain dyes forms the basis for several liver function tests.

Differentiate between "liver failure" and "hepatic coma."

Liver failure is a rapid deterioration of all functions of the liver, which initiates a vicious cycle, namely, fluid loss, anoxia, hemorrhage, metabolic aberrations, and specific organ damage. "Hepatic coma" represents but one of the manifestations of "liver failure" and is due to an abnormal concentration of metabolites (or other substances) in the central nervous system.

Give the classification of jaundice.

(*1*) *Hemolytic Jaundice:* Due to an excessive production of bilirubin (congenital hemolytic jaundice, icterus neonatorum, pernicious anemia, sickle-cell anemia, malaria, transfusion reactions, infections, etc.).

(*2*) *Hepatocellular Jaundice:* Decreased removal of bilirubin from the blood and escape of bilirubin from canaliculi into blood as a result of insufficiency of hepatic cellular function and obstruction of intrahepatic biliary passages (infectious hepatitis; hepatic necrosis; infectious mononucleosis; poisoning with sulfonamides, mercury, lead, chloroform, etc.; congestive heart failure; hepatitis due to any infection; etc.).

(*3*) *Obstructive Jaundice:* Damage or obstruction of extrahepatic biliary passages (biliary or pancreatic calculi, cholangitis, new growths of pancreas, ducts, or lymph nodes, etc.).

Is the gallbladder an essential organ?

Although the gallbladder is not classed as an essential organ, it nevertheless has definite functions, the most important being its storage capacity of bile in a concentrated form, which is discharged intermittently into the duodenum and is mixed with the pancreatic juices to initiate intestinal digestion. This release of bile by the gallbladder occurs as the stomach begins to secrete acid and to empty.

Discuss the functions of the pancreas.

(*1*) *Endocrine Function:* Insulin secreted by the islet cells is concerned with carbohydrate metabolism (diabetes mellitus, hypoglycemia). In addition, the pancreas probably secretes a lipotropic hormone (lipocaic).

(*2*) *Digestive Function:* The acinar tissue produces the pancreatic juices and is under both nervous (vagal) control, which stimulates a secretion rich in enzymes, and humoral (secretin) control, which produces a greater secretion, relatively rich in bicarbonate.

Discuss the role of the liver in the metabolism of estrogens.

The liver effectively removes estrogens from the systemic circulation by biliary excretion and metabolic degradation to less active and inactive compounds; the liver conjugates estrogens with glucuronic and sulfuric acids, converting them to water-soluble forms, which return to the systemic circulation and are excreted in the urine; and the liver may convert estrone to the more potent estradiol. An inadequate inactivation of estrogens by the liver has been held responsible for some of the most interesting physical signs often, but not invariably, found in patients with chronic hepatic disease: (1) loss of hair; (2) fine, soft skin; (3) testicular atrophy; (4) gynecomastia; (5) palmar erythema; (6) arterial spiders; (7) vascular dilatation or engorgement on face, on the buccal mucosa, in the nares, and in the conjuctivae.

RENAL SYSTEM

Discuss the functions of the kidneys.

The principal function of the kidneys is the formation of urine, which represents a by-product of their regulatory activities, namely, (1) the regulation of water and electrolyte balance and osmotic pressure of the body fluids, (2) the regulation of acid-base balance, and (3) the removal of metabolic waste products and certain toxic substances.

Enumerate the principal anatomical structures of the kidney.

(1) The glomeruli, containing both afferent and efferent vessels, which, in health, form a filter system. (2) The tubular system, in which occur both active absorption of materials which involves energy and the passive adsorption of fluid constituents. Glomerular fluid in general consists of blood constituents without protein. Those constituents such as sugar and others must be absorbed, and likewise fluid must be adsorbed.

(3) The collecting tubule drainage system, the importance of which is tremendous in infection; it is not important in the immediate function of the kidney unless infection spreads.

Discuss the fundamental mechanism involved in the excretion of urine.

(*1*) *Filtration and Reabsorption:* Blood flowing through the glomeruli under a positive pressure is filtered out into the glomerular capsule; the tubules actively and selectively reabsorb substances that the body needs to retain (glucose, amino acids, water, and electrolytes). Metabolites such as urea, uric acid, and creatinine, for which the body has no further use, are largely excreted.

(*2*) *Tubular Excretion:* Ammonia, hydrogen ions, organic acids, exogenous creatinine, potassium, and foreign substances (Diodrast, phenol red, para-aminohippurate) are excreted by the tubules.

(*3*) *Acid-Base Balance:* The largest renal factor in maintaining the volume and concentration of body fluids is tubular reabsorption of water and major electrolytes (Na^+, Cl^-, HCO_3^-). The kidneys efficiently eliminate or conserve either acid or base during the selective reabsorption of electrolytes. In the excretion of phosphate, the substitution of a hydrogen ion for a sodium ion permits the simultaneous excretion of acid and reabsorption of part of the sodium. If an excess of acids persists, ammonia is formed in the kidney and eliminated in place of sodium.

(*4*) *Endocrine Influences.* Adrenal corticosteroids are essential for the normal reabsorption of sodium, excretion of potassium, and normal diuresis of water; the antidiuretic hormone of the posterior pituitary inhibits the reabsorption of sodium and chloride and increases the reabsorption of water.

What is the function of the "artificial kidney"?

Extracorporeal hemodialysis by the "artificial kidney" has proved to be a valuable adjunct in the management of acute renal failure or lower nephron nephrosis, and in the treatment of acute poisoning due to certain drugs—such as barbiturates, bromides, and salicylates, substances that are not bound to tissue proteins. The primary objective is to give the patient with acute renal failure a slightly greater chance of surviving long enough to permit restoration of adequate renal function. This is achieved largely by removing from the blood certain accumulated products of metabolism, and by temporarily correcting certain fluid and electrolyte abnormalities associated with renal failure.

Describe the mechanism of micturition.

Irritation of the sensory nerves of the bladder when it is moderately distended excites the reflex in the vesicospinal center through the motor nerves of the bladder, causing contraction of the walls and expulsion of the contents after the sphincter of the urethra has been voluntarily relaxed. Evacuation is aided by voluntary contraction of the abdominal muscles and in men, toward the end of the act, of the bulbocavernosus muscle (accelerator urinae). The reflex may also be excited by irritation of other sensory nerves (tickling or warming the region of the knee, hearing the sound of running water).

What is the significance of the specific gravity of urine?

One of the most important characteristics of a normal kidney is its ability to eliminate the required quantity of solids regardless (within wide limits) of the amount of water available for their solution. Normally, urine of large volume (ingestion of excessive amounts of fluids) has a low specific gravity, that of low volume (ingestion of small amounts of fluids or loss of fluids through the skin or gastrointestinal tract) a high specific gravity. In the presence of renal damage, the ability of the kidney to concentrate urine is diminished (hyposthenuria) and, as the renal function impairment progresses, the kidney also loses its ability to dilute urine, which results in a relatively fixed specific gravity (above or below 1.010).

Give a test for measuring the excretory rate of the kidney.

The most commonly used test is the parenteral injection of phenolsulfonphthalein, which is excreted almost entirely by the tubules. The rate at which this dye appears in the urine depends on the rate of renal blood flow, the percentage removed from the blood during one renal circulation, and the rate at which fluid moves down the urinary tract. Conditions that interfere with one or more of these factors (renal disease, obstructive uropathies, oliguria, etc.) tend to slow the rate of excretion. Normally, 70 per cent of the injected dye is excreted in 2 hours and about 30 per cent in 30 minutes after the intravenous injection of 6 mg. of phenolsulfonphthalein.

Define lipuria.

Lipuria, fat in the urine, may be present in normal individuals after the ingestion of a high fat diet (alimentary lipemia) or after the administration of such substances as cod liver oil. Lipuria may also occur in association with the lipemia of diabetes mellitus and nephrosis, after fractures of long bones and extensive superficial injuries, and poisoning with phosphorus or alcohol.

Discuss the mechanism of glucosuria.

Excretion of abnormal amounts of glucose in the urine may be due to (1) increase in the amount of glucose entering the tubules per minute, which is the product of the minute volume of glomerular filtrate and the concentration of glucose in the filtrate, and (2) decrease in the glucose-reabsorptive capacity of the tubular epithelium, which is probably related to a specific enzyme mechanism involving phosphorylation ("renal" glycosuria, "lowered renal threshold" for glucose).

Define ketosis and ketonuria.

Ketosis is the term applied to the accumulation of excessive quantities of "ketone bodies" (acetoacetic acid, β-hydroxybutyric acid, and acetone) in the body; *ketonuria* refers to their excretion in excess in the urine. They may occur in a variety of clinical conditions that have as a common denominator an inadequate supply or utilization of carbohydrate: diabetes mellitus, carbohydrate starvation (vomiting, anorexia, starvation, etc.), hyperinsulinism, acute increase in metabolism (fever, hyperthyroidism, etc.).

What factors may cause an abnormal decrease in effective renal blood flow?

(1) Decrease in cardiac output or lowered arterial pressure (congestive heart failure, shock syndrome, etc.). (2) Organic disease of the renal vascular system (renal arteriosclerosis, arteriolosclerosis, glomerulonephritis, etc.). (3) Increased local resistance to the flow of blood, resulting from vasoconstriction of the afferent and/or efferent glomerular arterioles (early essential hypertension, systemic arterial hypotension). (4) Disease in the mass of functioning kidney tissue (polycystic disease, pyelonephritis, renal hypoplasia, tuberculosis, etc.).

Discuss the significance and causes of oliguria.

Oliguria, a decrease in urine volume, may aggravate renal functional impairment due to renal disease or may, of itself, produce renal insufficiency in the absence of intrinsic kidney damage.

Oliguria (or anuria) may be due to: (1) prerenal causes—excessive loss of water and electrolytes by extrarenal routes (prolonged vomiting or diarrhea, excessive sweating, profuse expectoration, etc.); (2) arterial hypotension, resulting in a reduced renal blood flow, giving rise to decreased glomerular filtration and tubular damage, as occurs in peripheral circulatory collapse (shock) after trauma, burns, acute hemorrhage, severe infections, etc.; (3) edema due to any cause; (4) kidney disease—diffuse glomerular damage (glomerulonephritis) of sufficient degree to reduce glomerular filtration to very low levels, or extensive tubular degeneration (poisoning, shock, lower nephron nephrosis); (5) urinary obstruction, which may be (*a*) intrarenal—the flow of urine through the tubules may be impeded as result of obstruction of the lumen by casts, crystals, etc., or (*b*) extrarenal, in which there is an increased back pressure as a result of bilateral lower urinary obstruction (calculi, stricture, tumor, prostatic enlargement, etc.), giving rise to a slower filtration because of increased capsular pressure.

Define proteinuria (albuminuria).

Under normal conditions, very little or no protein is eliminated in the urine because the glomerular capillary membrane of the kidney exists as a barrier between the blood plasma and the urine, allowing the passage of water and most crystalloids but not of colloids to which it is practically impermeable. However, in renal disease, the glomerular capillary membrane permeability is so increased that protein derived from plasma protein passes through into the urine. For the most part, the protein found in urine is albumin globin (pseudoglobulin and englobin) and fibrinogen, the proportion of each of these substances so eliminated by the kidney being determined by the relative size and viscosity of the molecules. Hence, albumin, having by far the lowest molecular weight and viscosity, is excreted in largest quantity, and fibrinogen, possessing the largest molecule, is eliminated in smallest amount, with the globulins occupying intermediate positions. Thus, the term "albuminuria," which has been universally employed, is not altogether synonymous with "proteinuria" in describing this condition.

What is functional albuminuria?

This condition includes a variety of cases of albuminuria that are apparently not dependent upon organic disease. It occurs most commonly in young individuals, is usually transient, the renal function is unimpaired, the urine is otherwise normal, and the subsequent medical history is negative. Included among this group of conditions are essential albuminuria, which includes orthostatic or postural albuminuria; cyclic albuminuria; intermittent albuminuria; and albuminuria of adolescence. In these cases the essential etiological factor is probably some disturbance of renal circulation either in the large vessels (movable kidney, lordosis) or in the renal arterioles (vasomotor instability). Temporary albuminuria may follow severe exercise, prolonged exposure to cold, severe mental strain, the ingestion of excessive quantities of native protein (egg albumin), and may occur during an uncomplicated pregnancy or just before menstruation.

LOCOMOTOR AND NERVOUS SYSTEM

Which systems are involved in locomotion?

(1) The skeletal supports of the body, the bones; (2) the joints between these osseous structures; and (3) the neuromuscular mechanism for moving these parts.

Discuss the functions of the joint cartilage.

The cartilage protects the subchondral bone from undue pressure by providing a cushioning effect, as well as a gliding surface for the opposing bone ends.

From what sources does cartilage derive its nourishment?

The chief source of nutriment comes from the synovial fluid, although some is derived from the blood supply of the subchondral bone and from the subsynovial vessels located at the junction of the capsule and cartilage.

What factors are concerned with changes in the physiology of the joint proper?

(1) Altered permeability of synovial and capsular tissue, which permits an increased passage of water, electrolytes, proteins, readily diffusible colloids, fibrinogen, antibodies, leukocytes, and probably enzymes into the joint space. (2) Disturbances of intra-articular metabolism, which affect chiefly the sugar and mucoprotein of joint fluid.

Differentiate osteoarthritis and neuropathic joint disease.

The articular disease is similar in the two conditions. Degenerative changes appear first in the cartilage with resultant softening, separation of the fibers, fissuring, and later disintegration. As the cartilage wears thin and bony proliferations develop as a result of friction, the function of the joint becomes disturbed, with associated pain. However, in persons with neurological disorders (tabes dorsalis, syringomyelia, pernicious anemia, uncontrolled diabetes) these degenerative changes usually progress more rapidly and, since the patient feels less pain, the continued unrestricted and unprotected use of the part results in extensive damage to cartilages and bone.

In what way does primary disease of the muscles interfere with the function of the locomotor system?

Myositis, an inflammatory reaction, causes pain and tenderness in the regions infected. These are aggravated by contraction of the muscle so that the patient avoids use of the muscle as much as possible and, in chronic cases, weakness may persist if atrophy is severe. Likewise, in the various muscular dystrophies, the abnormal function is due to weakness of the muscle.

Name some of the involuntary muscles and the function with which each is concerned.

The *uterus* is the organ for carrying the developing embryo and fetus. The muscle is used for the expulsion of the fetus at the end of intrauterine life.

The muscular wall of the *intestines* mixes and passes on the food received from the stomach.

The tunica media of the *arteries* contains many muscular fibers that control the supply of blood to the various parts of the body.

Define (*a*) tonic muscular contraction, and (*b*) clonic muscular contraction. Give an example of each.

A *tonic* muscular contraction is continuous, as in the action of the sphincter ani and other sphincter muscles.

Clonic muscular contraction is intermittent or remittent, like the jerking movements in a (clonic) convulsion.

What stimuli produce muscular contraction? What is the nervous mechanism of muscular contraction? Illustrate.

Stimuli producing muscular contraction are: normal (voluntary), chemical (automatic movements), thermal (reflex excitation), mechanical, and electrical.

Nervous Mechanism of Muscular Contraction: The motor impulse starts from the motor nerve cell and passes down the motor neuraxon to the motor end-plates, where the muscle cells are stimulated to contract. One stimulus would simply cause a muscular twitch, but normally in a muscular act a series of impulses is sent from the nerve centers to keep the muscles in a voluntary tetanus. *Example:* In raising the foot, the motor impulse starts in the cerebral gray cells of the rolandic area, passes down to the cells in the anterior horn of the opposite side in the lumbar cord, then out through the sciatic nerve to the motor end-plates of the muscles required to lift the foot, which in turn stimulate the muscular fibers.

Describe nerve cells and fibers.

Nerve cells or *neurons* are nucleated masses of granular protoplasm, with one or more protoplasmic prolongations called *dendrons* or *dendrites.* Most nerve cells are supplied with a long fiber or *axis-cylinder.*

Nerve fibers are medullated or nonmedullated:

The *nonmedullated, gray fibers* are surrounded by *neurilemma* or the sheath of Schwann. They are most numerous in the sympathetic system.

The *medullated, white fibers*—axis-cylinder or neuraxons—are surrounded by *myelin* or the white substance of *Schwann* (also called medullary sheath), which in turn is covered by the sheath of Schwann or neurilemma. They are found principally in the cerebrospinal nerves. Here and there under the sheath of Schwann are found the *nodes of Ranvier,* annular constrictions about which the myelin is lacking.

Define (a) afferent, (b) efferent, (c) trophic, (d) inhibitory, (e) motor and (f) vasomotor nerve fibers.

(*a*) Nerve fibers carrying impulses to the central nervous system from the various parts of the body. Impulses received on the retina are carried to the brain by the optic nerve.

(*b*) Nerve fibers carrying impulses from the nerve cell to the various parts of the body. The facial nerve carries motor impulses from the corresponding center in the brain to the muscles of expression.

(*c*) Nerves influencing the nutrition, metabolism, and growth of the tissues to which they are distributed. Lesions involving destruction of the trophic nerves and centers cause atrophy of the corresponding tissues (muscles, cartilage in joints, and bones).

(*d*) Nerves carrying impulses that tend to suppress or diminish a movement or secretion already present.

(*e*) Nerves carrying motor impulses from the brain or cord to the various muscles of the body.

(*f*) Nerves carrying impulses that control the muscular tone of the walls of blood vessels.

Define (a) neurotmesis, (b) axonotmesis, and (c) neurapraxia.

(*a*) Neurotmesis is the complete anatomical division of a peripheral nerve with loss of conduction of both efferent and afferent impulses.

(*b*) Axonotmesis is a loss of function of the axons, or nerve fibers, with resulting peripheral degeneration of the conducting structures of the nerve, but the supporting tissues, the epineurium and endoneurium, are preserved. Spontaneous recovery may occur and during regeneration the nerve fibers follow their original channels. (*c*) Neurapraxia is a transient block or interruption of continuity, due to compression or blows by blunt instruments, which does not produce complete paralysis and is not accompanied by peripheral degeneration.

Give the various causes of nerve injuries.

Nerves may be injured by trauma, pressure, chemical or toxic influences, interruption of blood supply, infectious processes, or deficiency in substances normally required for nerve metabolism.

Give two examples of disorders of physiology at the neuromuscular junction.

(1) Myasthenia gravis, which results from either a failure of acetylcholine to form or a defect in the amount of acetylcholine at the motor nerve ending. (2) Familial periodic paralysis, which is attended by a fall in the potassium and phosphate content of the blood serum.

Discuss the role of oxygen, lactic acid, and glycogen in the intermediary metabolism of muscle.

There are two phases in the intermediary metabolism of muscle:

Anaerobic Phase: During this phase work is done by the muscle. Oxygen is not used. Lactic acid is produced from glycogen through the intermediation of a phosphorus-sugar compound, hexosephosphate.

Aerobic or Recovering Phase: In this phase oxygen is consumed, about one fifth of the lactic acid is oxidized to CO_2, presumably to furnish energy for the resynthesis of the remaining four fifths lactic acid to glycogen.

Define electrotonus, and explain the law of contraction operative when a closing and opening current is applied to the muscles.

If a living nerve is traversed throughout a definite length by a constant electric (polarizing) current, the muscle passes into a condition of altered irritability designated *electrotonus.* At the positive pole, or anode, the irritability is diminished and *anelectrotonus* prevails. At the negative pole, or cathode, it is increased—*catelectrotonus.*

(1) On closing the circuit stimulation occurs only at the cathode, at the moment when catelectrotonus develops. (2) On opening the current stimulation takes place only at the anode, at the moment when an electrotonus disappears. (3) The stimulus attending the development of catelectrotonus is stronger than that caused by the disappearance of anelectrotonus.

What is meant by the condition of tetanus in a muscle?

When a muscle goes into a state of continued contraction it is said to be tetanized.

What is meant by the "all-or-none" property of muscle?

A stimulus, if effective, will elicit the maximal response under the conditions existing at the time of stimulation. This principle applies to all types of muscle fibers: striated, smooth, and cardiac musculature. In striated muscle a stronger stimulus may stimulate more motor nerve fibers than a weak one, hence the corresponding muscle will have more fibers stimulated. The all-or-none principle holds for the individual fiber in striated muscle.

What is tonus; what is its significance?

Tonus is dependent upon a series of efferent impulses from reflex arcs to skeletal musculature keeping certain muscle bundles in each muscle group in a state of contraction. As one bundle tires, another takes up its function. The basic nerve pattern is influenced by higher brain centers. The maintenance of posture and balance are dependent upon tonus.

What is the refractory period?

The refractory period is the time interval elapsing between one contraction of a muscle fiber and another contraction; during this interval a stimulus will fail to produce a contraction.

Describe the functions of spinal nerves.

The spinal nerves carry the afferent and efferent impulses of the body and of the back of the head to and from the central nervous system. Among the afferent impulses are those of pain, temperature, tactile, pressure, and muscular sense. Among the efferent are the motor, trophic, secretory and vasomotor.

Name the principal centers of organic function in the medulla oblongata.

Respiratory, cardio-inhibitory, cardioaccelerator, vasomotor; centers for salivation, mastication, deglutition, vomiting; and the diabetic center.

What are the functions of the spinal cord?

The spinal cord is the great motor and sensory pathway to and from the periphery. In the anterior horns are found the cells concerned in the muscular reflexes and also the trophic centers for the muscles. Besides the muscular reflex centers, the cord contains the following centers: Anospinal, vesicospinal, genitospinal, uterospinal, sweat, minor vasomotor, and possibly ciliospinal.

Explain the functions of the principal columns of the spinal cord.

The anterior and lateral columns—the *pyramidal tracts*—convey motor impulses to the voluntary muscles of the same side. Sensation, pain impressions, sensation of heat and cold, and muscular and pressure sensations are conveyed through the *posterior columns.*

Discuss briefly the metabolic processes involved in muscular contraction.

One of the proteins present in muscle fibrils, actin, is found in two forms. G-actin is a globular protein; under the influence of ATP, it undergoes rearrangement and polymerization to F-actin, a fibrous protein. F-actin and myosin combine in a ratio of about 3 to 1 to form actomyosin. This reaction requires the Mg ion. Actomyosin then contracts, using the energy from ATP, which is thus degraded to ADP. Muscle glycogen seems to be an important source of energy for these reactions. If the process is going on rapidly and insufficient oxygen is present, lactic acid may be formed temporarily. Otherwise, glycogen breaks down through pyruvate in the usual way. In either case, energy is released, which aids in the regeneration of ATP from ADP. A reserve of ready energy is available from the breakdown of phosphocreatine to creatine. Further energy may come from the breakdown of ADP to AMP. Myosin has the peculiar property of promoting the breakdown of ATP to ADP, and is thus an "ATP-ase." It is not clear just what part this property plays in physiological muscular contraction. The above series of reactions depends upon a proper balance of electrolytes, especially Mg^{++}, Ca^{++}, and K^{+}.

What are the principal constituents of bone?

Bone may be said to consist of about 60 per cent of inorganic salts ("bone salt"), primarily a calcium magnesium phosphate similar to the mineral hydroxyapatite. Smaller quantities of sodium, magnesium, fluorine, strontium, carbonate, and citrate are also present. Calcium makes up about 36 per cent, magnesium 0.6 per cent, and phosphorus 16 per cent. In the matrix of this mineral material lies about 40 per cent of organic matter. This is a tough mixture of proteins, primarily ossein, a form of collagen. Smaller proportions of osseoalbuminoid (an elastin) and osseomucoid (a glycoprotein) are also present. Before drying, bone may contain up to 25 per cent water in association with both organic and inorganic elements. The bone marrow present in many bones is often high in lipids, especially in the more inactive, less cellular portions of the marrow.

What are the important chemical components of muscle? What are the loci of these components within the cell?

Muscle tissue is composed of cells containing muscle fibrils amid a sarcoplasm. The cells are surrounded by a varying amount of stroma. The fibrils contain two proteins, myosin and actin, which are concerned in muscular contraction; these account for about half of the total muscle protein. The proteins in the sarcoplasm are less well known, but include myoglobin, myogen, and a mixture of globulins. Myoglobin is somewhat similar to hemoglobin and may act as a storage place for oxygen. Myogen is a mixture of proteins, and contains certain enzymes. Muscle also contains relatively large amounts of glycogen, which is an energy source. Certain soluble compounds are present, the "extractives" of muscle. These include various anions and cations, a proper balance of which is needed for normal muscle function. ADP, ATP, adenylic acid, phosphocreatine, creatine, creatinine, DPN, TPN, and other compounds of metabolic significance are also present. Two compounds of unclear function are among the extractives: carnosine and anserine, which are dipeptide-like substances.

Briefly discuss the composition of cartilage.

Cartilage is a poorly vascularized tissue composed of a matrix of protein with infrequent cartilage cells dispersed therein. The matrix consists mainly of collagen, with smaller amounts of chondroalbuminoid (similar to elastin) and chondromucoid. The latter is a glycoprotein with chondroitin sulfuric acid as a prosthetic group. On hydrolysis, chondroitin sulfuric acid gives glucuronic acid, acetic acid, sulfuric acid, and galactosamine. Cartilage may ossify, in which case it is found to contain glycogen, which appears to play some part in the process.

What is the role of vitamin A in the visual cycle?

Vitamin A is responsible for the ability of the eye to see in dim light. The retina has two components directly connected with transmitting visual impulses to the optic nerve, namely the cones and the rods. The cones are responsible for color vision and vision under normal light. The rods are responsible for the ability of the eye to see in dim light and for the familiar ability of the eye to adapt itself gradually to very dim light.

The process of adaptation to dark is a chemical one and consists in the function of photosensitive chemicals in the retina which, on exposure to light, break down and initiate a nerve impulse. The photosensitive chemical of the rods is known as *rhodopsin* (visual purple). Rhodopsin is a combination of a protein and vitamin A. Upon exposure to light, rhodopsin breaks down to form *retinene* (visual yellow), which initiates a nerve impulse. This reaction is reversible and may be diagrammed as follows:

Vitamin A + Protein = Rhodopsin
DARK ↑ ↓ LIGHT
Retinene
↓
Nerve impulse

How is normal body temperature regulated and sustained?

It is regulated chiefly by the nervous mechanism of heat or *thermotaxis*. There are *thermogenic* and *thermolytic* centers. The principal thermogenic centers (automatic, reflex, or general) are found in the cord, probably in the anterior horn. The thermolytic centers are five in number: vasomotor, sweat, respiratory, cardiac, and pilomotor. Dissipation of heat is effected by dilatation of the surface vessels, increased sweat production, acceleration of the respiration, and the raising of the hair. Sweating is probably the most important factor in heat dissipation.

Discuss the chemical composition and metabolism of nervous tissue.

Nervous tissue contains from 70 to 85 per cent water. The solid matter varies; the white matter contains much more lipid than the gray matter. This lipid is a mixture with little neutral fat present. It consists of phospholipids, glycolipids and cholesterol in decreasing amounts. The phospholipids are mainly cephalin, lecithin, and sphingomyelin. Much of this lipid is in the myelin sheaths of the axons. Nervous tissue metabolizes glucose, perhaps exclusively. A small amount of glycogen is present in nervous tissue, but is not abundant enough to be much of a reserve. The acetylcholine content of nervous tissue is high; it is an important chemical mediator between nerve cells.

What are the respective functions of the anterior and of the posterior cornua of the spinal cord?

The anterior cornua are motor in function and contain the trophic centers for the muscles. The posterior cornua are mostly relay stations on the sensory pathway.

Where is the respiratory center? Where is the center of defecation?

The respiratory center is situated in the *floor of the fourth ventricle*, between the nuclei of the vagus and spinal accessory nerves. The center for defecation—Budge's anospinal center—is situated in the spinal cord, at the level of the *fifth* dorsal vertebra.

Give the function of the epiglottis.

Assists in preventing the entrance of food into the larynx during deglutition and influences the *timbre* or quality of the voice (clear or muffled); it does not affect pitch.

Describe the position of the vocal cords during phonation and name the factors concerned.

The chink of the glottis during phonation is narrowed, the arytenoid cartilages are approximated, and the vocal cords are stretched. The arytenoid muscle approximates the arytenoid cartilages and, with the help of the lateral crico-arytenoids and the internal part of the thyroarytenoids, closes the glottis. The vocal cords are made tense by the crico-thyroids and external part of the thyro-arytenoids.

Define aphonia and aphasia. Give the cause of these conditions.

Aphonia is the loss of voice or power of phonation. It is due to paralysis of the motor nerves of the larynx, wounds, tumors, aneurysm, rheumatism, overexertion, hysteria, or edema of muscles.

Aphasia is the inability to give the proper word symbol. Motor aphasia is due to a lesion of the left lower frontal convolution or of the fibers coming from it.

What is the location of the center for articulate speech?

Broca's convolution, the left lower frontal in right-handed people.

What causes the difference in pitch between male and female voices?

The pitch is inversely proportional to the length of the vocal cords; it is, therefore, higher in women and children than in men.

Describe the action of the vasomotor nerves.

The vasomotor nerves contain *pressor* (constrictor) and *depressor* (dilator) fibers. Irritation of the pressor fibers causes stimulation of the vasomotor center in the medulla and increased tone in the blood vessels (vasomotor tone). Irritation of the depressor fibers causes reflex diminution of the irritability of the center. The vasomotor nerves serve to regulate the blood pressure and the amount of blood going to a part; they also contribute to the regulation of the body temperature by increasing and diminishing evaporation from the surface.

Define reflex action and give examples.

Action resulting from an afferent impulse, followed by an efferent impulse, without the intervention of the higher cerebral centers. Reflex action is independent of the will. *Example:* Tapping the tendon of the quadriceps extensor is followed by a reflex contraction of the muscle (knee jerk). The pupils contract under the influence of light and accommodation.

Explain the physiologic circuit essential to a reflex action.

A centripetal fiber, a ganglionic nerve center in the gray matter, a centrifugal fiber (cord or medulla), and muscle or other peripheral organ supplied by the efferent nerve. This is called the *reflex arc.*

Mention (*a*) the superficial reflexes, and (*b*) the deep reflexes.

(*a*) Abdominal, cremasteric, plantar, palpebral, palatal, and corneal-conjunctival reflexes.

(*b*) Knee jerk or patellar reflex, ankle clonus, bicipital reflex, chin reflex, and pupillary reflex.

What test should be applied to ascertain the integrity of (*a*) the superficial reflexes, and (*b*) the deep reflexes?

(*a*) The plantar reflex—movement of the toes on stroking the sole of the foot; the cremasteric—retraction of the testicle on stroking the inside of the thigh; the conjunctival—closure of the eyelid on touching the conjunctiva; and many others.

(*b*) The integrity of the deep reflexes is best ascertained by testing the knee jerk (see above) or the bicipital reflex—contraction of the biceps on tapping the tendon at the elbow.

What is the physiologic significance of the normal patellar reflex and through what nerves is it accomplished?

Health: It is present in all but about 5 per cent of normal individuals. *Afferent path:* posterior root of fourth lumbar nerve. *Efferent path:* fourth and fifth lumbar nerves.

What influence has the nervous system on the process of secretion?

The nervous system controls the process of secretion by the various secretory centers and nerves and by regulating the blood supply of the various organs of the body.

How is the sensation of pain produced?

Stimulation of the special endings of the pain nerves in the skin or stimulation of the trunk of the nerve causes an impression to be sent to the special area of the brain presiding over pain sensations. Stimulation of this center results in the subjective sense of pain.

Describe the origin of a tear as the result of pain.

The pain causes reflex stimulation of the lacrimal gland, followed by increased secretion. More secretion is produced than can be carried off by the lacrimal canal and the excess overflows from the conjunctival sac as tears.

Describe the characteristic effects of stimulation of efferent sympathetic nerves.

Cervical Sympathetics: Dilatation of pupils (mydriasis); retraction of the upper lid; exophthalmos; constriction of blood vessels in head and neck; secretion of sweat glands.

Thoracic Sympathetics: Acceleration of the heart; dilatation of the bronchi; constriction of the pulmonary arteries and dilatation of the coronary arteries.

Abdominal Sympathetics (Including the Splanchnic Nerves): Peristalsis is diminished and the sphincters are stimulated; the splanchnic blood vessels are constricted; the bladder muscle is relaxed, but the sphincter is stimulated; the secretion of medullary layer of suprarenal glands is increased; the spleen is stimulated and contracts; the uterus, fallopian tubes, and vas deferens receive both motor and inhibitory stimuli; the peripheral blood vessels are constricted.

What are the functions of the parasympathetic nervous system?

Vagus nerve: slows the heart; constricts the coronary arteries; constricts the bronchi; increases peristalsis in the stomach and intestine; stimulates secretion in the stomach and pancreas; relaxes sphincters.

Oculomotor nerve: contracts the pupil (miosis).

Facial nerve: stimulates the lacrimal, submaxillary, and sublingual glands.

Glossopharyngeal nerve: stimulates the parotid gland.

Sacral nerves: constrict the bladder, colon, and rectum with relaxation of the sphincter muscles; stimulate the prostate and cause erection of the penis.

Peripherally vasodilatation occurs, with stimulation of the sweat glands.

State the functions of the fifth cranial nerve.

The fifth nerve is the *sensory nerve* of the face, mouth, and nasal cavities, and the *motor* nerve of the muscles of mastication.

What is the function of the sixth (abducens) nerve?

The *abducens* is the motor nerve of the external rectus.

Give the physiologic properties of the facial nerve.

The facial nerve is the motor nerve for the muscles of expression of the face. Through the fibers of the *chorda tympani* and the *lingual* nerve, it also subserves the sense of taste in the tip and margin of the tongue. The gustatory fibers of the chorda tympani originate in the glossopharyngeal nerve and enter the facial through the intermediary portion of Wrisberg.

What would be the effect of paralysis of the seventh cranial nerve (portio dura) on the right side?

Paralysis of the right half of the face.

Name the functions of the chorda tympani, sufficiently detailing each to define its character clearly.

The chorda tympani contains *sensory* (also tactile and thermic) and *gustatory* fibers for the anterior portion of the tongue; *secretory* fibers for the sublingual and submaxillary glands; and *vasodilator* fibers for those glands and for the anterior two thirds of the tongue.

What is the function of the glossopharyngeal nerve?

The glossopharyngeal is the *nerve of taste* for the posterior third of the tongue and the lateral portion of the palate. It supplies *motor* fibers to the stylopharyngeus muscle and *secretory* fibers to the parotid gland. It is the *sensory* nerve for the posterior third of the tongue, the tonsils, the anterior palatine arches, the soft palate, and a portion of the pharynx.

What are the functions of the vagus nerve?

Among its many functions the vagus is motor and sensory to the larynx; motor to the pharynx and esophagus; motor, sensory, and secretory to the stomach; *inhibitory to the heart;* motor and sensory to the lungs; and sends some filaments through the sympathetic system to the pancreas, liver, and intestines.

What is the function of the superior laryngeal nerve?

The superior laryngeal is the *motor* nerve of the cricothyroid muscles and the *sensory* nerve of the larynx.

Give (a) number of spinal nerves, and (b) function of anterior and posterior roots.

(*a*) Thirty-one. (*b*) Motor and sensory respectively (Bell's law).

State the function of the anterior spinal nerve roots. How is the function proved?

They supply *motor fibers* to all the striated voluntary muscles of the trunk and extremities and to certain organs—the bladder, uterus, and skin; *vasomotor* fibers to the vessels; *sweat* fibers to the sweat glands; and *trophic* fibers. Section of the anterior roots causes motor paralysis of the parts that they supply. Irritation of the peripheral ends causes contraction of the muscles they supply. Irritation of the central ends has no effect; no sensation is felt.

Enumerate the physiologic advantages of natural sleep and state at what period of life the least sleep is required.

(*a*) The fall in the blood pressure and the relaxation of the vasomotor tone, aided by the recumbent position, ensure the most complete rest for the heart. All the tissues of the body, especially the nervous tissues, have an opportunity to recuperate, and waste matter is carried off.

(*b*) It is during adult life that the least sleep is required.

Describe the offices and the characteristics of the gray matter of the brain.

The gray matter of the cerebral cortex is arranged in six alternate gray and white layers, the most important of which is the deep gray layer of large pyramidal cells. The gray matter of the cerebrum is the center of sensation, volition, and ideation; that is, it receives the sensation, sends out all voluntary impulses, and is the part of the nervous system in which thought goes on.

What differences of function exist between the white and the gray matter of the encephalon?

The *gray matter* is composed of cells which are the terminals that receive sensation, classify the knowledge thus received, and send out impulses. The *white matter* is made up of fibers that transmit the impulses connecting the cells with each other and with the periphery.

What portion of the cerebrum comprises the motor area?

The motor area is found along the *central Rolando's fissure,* in the ascending frontal, ascending parietal, and paracentral convolutions, and contiguous parts of the superior frontal.

From what portions of the cortex cerebri do the arm, face, and leg receive their motor impulses?

The *central fissure* in the ascending frontal, ascending parietal, and paracentral convolutions. The leg center is the uppermost, the arm center next, and the face center the lowermost.

Locate in the brain the seat of the special senses of sight, hearing, and smell.

Sight has its seat in the gyrus angularis, the *cuneus,* and in the occipital lobes; hearing in the *superior temporal convolution;* and smell in the *uncus.*

Describe the paralysis resulting from a destructive lesion which involves the posterior limb of the internal capsule.

Paralysis of the opposite side of the body with redness, elevation of temperature, swelling, sweating, and rapid trophic changes (decubitus) in the affected extremities. Contractures subsequently occur in the paralyzed muscles, and abnormalities of the skin and cutaneous structures appear.

What are the effects of the removal of the cerebrum in the lower animals?

A decerebrated animal loses all power of voluntary movement, remaining quiescent until some external stimulus brings out a reflex movement. Thus, the animal will not take food that is placed before it; but if the food is placed in its mouth, it will swallow it. If turned on its back it will right itself. It shows no fear.

What is the function of the cerebellum?

Coordination of muscular movements. It also adds to the strength of voluntary movements, and increases the tone of the muscles during rest.

What would be the effect of a transverse section of (a) the anterior root of a spinal nerve, and (b) the posterior root of a spinal nerve?

(*a*) Transverse section of the *anterior root* would cause motor paralysis of the muscles supplied, and finally atrophy of the muscles. (*b*) Transverse section of the *posterior root* would cause loss of sensation of the part supplied.

What is the effect of division of the third cranial nerve?

Loss of accommodation, ptosis, external or divergent squint, and diplopia.

Which of the cranial nerves are nerves of special sense? Give the origin and function of each nerve mentioned.

Olfactory: origin by three roots, the external from the amygdaloid nucleus and adjacent portion of the cortex; the middle from the anterior commissure; and the internal from the gyrus fornicatus. *Function:* smell.

Optic: origin by two roots, external and internal geniculate bodies, pulvinar of the optic thalamus, and superior corpora quadrigemina. *Function:* sight.

Auditory: superficial origin, lower border of pons; deep origin by two roots, a lateral and a mesial. The lateral root is the true nerve of hearing and arises chiefly from the accessory nucleus. *Function:* hearing.

(a) What three cranial nerves are for special sense? (b) What six are exclusively motor? (c) What three are compound?

(*a*) Olfactory, optic, and auditory.

(*b*) Oculomotor, trochlear, abducens, vagus, accessory, and hypoglossus,

(*c*) Trigeminal, facial, and glossopharyngeal.

State the function of the nervus opticus, and explain by description or diagram the distribution of the fibers composing the chiasm and the effect thereof upon vision.

The nervus opticus is the nerve of the special sense, sight. At the *chiasm* the inner half of each optic nerve crosses to the opposite side; therefore, in loss of function of one optic nerve, from injury or pressure back of the chiasm, there is blindness of the temporal side of the retina of the same eye and of the nasal side of the opposite eye.

Give the foramen of exit, the distribution, and the function of the oculomotor nerve.

The oculomotor nerve leaves the skull through the sphenoidal fissure. It supplies *motor* filaments to the superior, internal, and inferior recti, the inferior oblique, the levator palpebrae superioris, the ciliary muscle, and constricting fibers of the iris. Its *function* is motor.

Describe the Babinski reflex and explain its significance.

Extension of the toes, instead of flexion, after irritation of the sole of the foot. It occurs in lesions of the pyramidal tract and indicates some organic lesion of the motor tract. The phenomenon is present in normal children up to the age of two.

What is ankle clonus?

A vibratory movement of the foot obtained by supporting the tendo achillis with one hand while the foot is strongly flexed with the other. It is rarely obtained in health, but is often marked in hysteria and in lateral sclerosis.

What conditions are necessary for properly exercising the sense of smell?

The odoriferous substances must be volatile, the air in the nasal cavities must be in motion, and the olfactory apparatus must be in a normal condition.

Name and locate the papillae of the tongue.

Circumvallate papillae near the base of the tongue, in two rows, forming a V, 7 to 12 in number. *Fungiform* papillae situated in front of the circumvallate and irregularly distributed on the dorsum, sides, and tip of the tongue. *Filiform* papillae, thickly scattered over the entire organ in front of the circumvallate.

What nerves are concerned in taste?

The *lingual* nerve, a branch of the fifth cranial, supplies gustatory fibers to the tip and margins of the tongue. The gustatory fibers are obtained from the chorda tympani, which are given off to the tongue as the nerve runs in the lingual. They originate in the facial nerve. The glossopharyngeal supplies gustatory fibers to the posterior third of the tongue, the lateral portion of the soft palate, and the glossopalatal arch.

Describe the nerve arrangements on which the sense of touch depends.

The tactile fibers are contained in the sensory nerve trunks and their terminations; the tactile corpuscles of Meissner, in the skin (corium); the corpuscles of Vater and Paccini, in the subcutaneous tissue; Krause's longitudinal end-bulbs, in the conjunctiva, the floor of the mouth, the lips, the nasal mucous membrane, etc.

What special diagnostic tests may aid in the evaluation of disease of the spinal cord?

Clinically, the presence of either local tenderness or muscular rigidity may signify the level of the pathological process. If either the anterior horn cells or motor roots are involved and if there are fascicular twitchings, electromyography assists in the localization of lesions. Dermometry and the sweating test may also prove valuable aids in localization. Spinal puncture, roentgenographic examinations, myelography, and sometimes myeloscopy may be necessary for the diagnosis and localization of spinal-cord lesions.

Discuss the syndrome of the herniation of the medulla and the cerebellar tonsils into the foramen magnum.

This syndrome is characterized by profound bradycardia, slow or rapid respirations, fall or marked rise in blood pressure, soaring temperature, unconsciousness and death. It may take place precipitously after the removal of cerebrospinal fluid by lumbar route in the presence of increased intracranial pressure, especially if the increased pressure is caused by posterior fossa tumors or abscesses.

Define Argyll Robertson pupil and name a disease in which it is one of the diagnostic symptoms.

A pupil that fails to respond to light, but accommodates for distance. Tabes dorsalis. In addition, pupils of this type may also be found in multiple sclerosis, encephalitis, diabetes mellitus, senile vascular conditions, and neoplasms of the pineal body or the posterior portion of the third ventricle.

What is the value of electroencephalography in the diagnosis of intracranial disease?

It is of most value in the interpretation and diagnosis of epilepsies, in the localization of focal cerebral disorders, in the study of the effects and possible sequelae of head injuries, in distinguishing between organic and nonorganic psychological disturbances, and has contributed a great deal to our current concepts of cerebral physiology.

Describe color blindness and name the colors which the subject commonly fails to distinguish.

The inability to recognize certain colors, usually red and green.

Locate the visual center.

The exact location is in dispute, but the weight of evidence is in favor of the *cuneus*, or upper portion of the occipital lobe. Accessory centers are probably present in the external geniculate body, the pulvinar of the optic thalamus, and the superior corpus quadrigeminum.

What is the condition of the eye in myopia? How may it be corrected?

In myopia the eyeball is longer than normal anteroposteriorly, and the rays of light are brought to a focus in front of the retina. The error can be corrected with a *concave lens*.

Describe the rods and cones of the retina.

The *rods* and *cones*, visual cells or *neuro-epithelium*, form the external coat of the retina and are separated from the choroid by pigment. They are absent at the entrance of the optic nerve. The rods are more numerous than the cones but are absent in the *macula lutea*, where cones alone are present. The outer portions of the rods contain a red pigment, the *visual purple*. The cones are shorter than the rods and contain no purple. The rods and cones are the only parts of the retina that are sensitive to light and constitute the active, receptive organ of sight.

Name the organs of the special senses.

The eye, the ear, the upper portion of the nasal cavities, the taste bulbs on the tongue, and the tactile end-organs.

What are the movements of the eyeball? Mention the muscles concerned in each of the movements.

Protrusion—muscular fibers in the capsule of Tenon.

Retraction—effected by tightly closing the lids or by paralysis of the muscular fibers of the capsule of Tenon.

Upward rotation—superior rectus and inferior oblique.

Downward rotation—inferior rectus and superior oblique.

Inward rotation—internal rectus.

Outward rotation—external rectus.

Rotatory rotation—both oblique muscles.

Describe the different coats of the eye and give the functions of each.

(1) *External* or *fibrous coat*, formed by the sclerotic and cornea, consisting of fine connective-tissue fibers. The *cornea* is transparent, the sclera white and opaque. The *sclera* is almost avascular, except for a large venous sinus at the corneal junction—the canal of Schlemm. The cornea contains no blood vessels ex-

cept at its periphery. By virtue of its transparency it admits the rays of light and, by its convexity, takes part in the refractive mechanism of the eye. The sclera is the protecting coat of the eyeball.

(2) *Middle* or *vascular* coat containing the uveal tract, iris, ciliary body, and choroid. The *choroid* forms the posterior part of the tract and contains pigment and blood vessels. In front of the choroid is the *ciliary body,* which also contains blood vessels, and the *ciliary muscle,* the muscle of accommodation. The anterior part of the uveal tract is formed by the iris, which acts like a diaphragm, cutting off the marginal rays and regulating the amount of light that enters the eye.

(3) *Internal* or *nervous coat*—the *retina*—containing the rods and cones (the neuro-epithelium), which are sensitive to light.

Name the refracting media of the eye and the effect that each has on the rays of light.

The cornea, aqueous humor, crystalline lens, and vitreous body. They all converge the rays of light in the following order of potency: crystalline lens, vitreous body, aqueous humor and cornea.

Describe the crystalline lens and state its relations and functions.

The *lens* is a biconvex, transparent body enclosed in a hyaline, elastic capsule. The posterior surface is more convex than the anterior. The lens is suspended within the globe by a suspensory ligament, the *zonule of Zinn,* attached to the capsule and swung from the ciliary processes. The outer portion or *cortex* is softer than the central portion or *nucleus,* which is quite dense. The lens comes in relation in front with the aqueous humor and pupillary border of the iris; behind, with the anterior surface of the vitreous, which receives it in a cuplike depression; peripherally, by the suspensory ligament, with the ciliary region. The crystalline lens is the organ of accommodation, which refracts the entering rays of light by altering its convexity.

What are the functions of the iris?

The iris is a circular muscular membrane or curtain with a round central opening. Its functions are: (1) to cut off the marginal rays like the diaphragm in the microscope and thus render vision more distinct; (2) to regulate the amount of light that enters the eye by contracting under strong illumination and relaxing (dilating the pupil) when the light is feeble; and (3) to assist the action of the muscle of accommodation.

Account for the contraction and dilatation of the pupil.

It is a reflex phenomenon regulating the amount of light that enters the eye and sharpening the image for near vision. The iris contains two sets of fibers; circular or contracting (*sphincter iridis*), and radiating or dilating (elastic) fibers.

Of the functions of vision, what is understood by accommodation?

The act of increasing the curvature of the anterior surface of the crystalline lens to focus near objects on the retina.

How is accommodation in the eye accomplished?

At rest, the lens is held flat against the vitreous body by the traction of the stretched zonule of Zinn, which is attached to its margin. When the ciliary muscle contracts to focus for near objects, it draws the margin of the choroid forward, and the zonule, which is in intimate relation with it, is relaxed and allows the lens, by virtue of its elasticity, to assume a more convex form (it becomes thicker). The posterior surface does not take part in the increase of curvature.

Define myopia, hypermetropia, and astigmatism. State the cause of each condition.

Myopia is a visual defect in which parallel rays of light are focused in *front* of the retina. The usual cause is an increase in the length of the anteroposterior diameter of the eye.

In *hypermetropia* parallel rays of light are focused *behind* the retina. It is generally caused by a shortening of the anteroposterior diameter of the eye.

Astigmatism is an error of refraction in which rays of light in the various meridians cannot be united at a single point. The rays that pass through the vertical meridian come together first, while the rays passing through the horizontal meridian are brought together in a more posterior plane (*regular astigmatism*). The error is generally due to irregularities in the curvature of the cornea, sometimes of the lens.

Give the mechanism of the organ of hearing.

The sound waves are collected by the auricle or external ear and conveyed through the external auditory meatus to the *membrana tympani,* or *drumhead,* which separates the meatus from the middle ear. A chain of minute bones, the *auditory ossicles—malleus, incus,* and *stapes*—occupy the middle ear and connect the drumhead with the internal ear. The sound waves impinging upon the drumhead set up vibrations in the membrane, which are transmitted by the chain of ossicles to the endolymph of the *labyrinth* of the internal ear. These vibrations in the endolymph are transmitted to the *organs of Corti,* which are contained in the scala media of the internal ear and form the special receptive apparatus of hearing. The auditory impressions are then conveyed to the auditory center in the cerebrum by the cochlear branch of the auditory nerve.

Describe the olfactory apparatus. What part of the olfactory apparatus is the seat of smell?

The upper portion of the nasal cavities contains the nerve endings of the olfactory nerve. These are specialized cells provided with small, hairlike processes. From these cells the olfactory nerve passes through the olfactory bulbs to the cerebrum, ending in the *uncus* of the same side.

INFECTION AND ALLERGY

What factors determine the severity of a particular infection?

The severity of any particular infectious disease varies with four factors: (1) the number of invading organisms, (2) the virulence of the organisms, (3) the tissue adaptability of the infecting agent, and (4) the resistance of the host.

Discuss the mechanisms by which latent infections may be converted into active disease.

While there is little knowledge of the precise mechanisms by which latent infections can be converted into active disease, it seems apparent that certain factors, such as nutritional, metabolic, and hormonal disturbances, play a role in the alteration of the metabolism of infected hosts. As an example of this, most organisms are taken up by phagocytic cells as soon as they are introduced into the body and later are released into the extracellular environment of the necrotic lesion. These leukocytes, in turn, can produce large amounts of lactic acid and it is probable that the intracellular pH, following a phagocytosis, is rather low. Similarly, it is certain that the pH of inflammatory exudates is very acid, in part at least as a result of the local accumulation of lactic acid produced by inflammatory cells. Furthermore, in vitro suspensions of many bacterial species are sterilized more rapidly in acid reactions in media containing lactic acid than in solutions containing other acids. Thus, lactic acid possesses antibacterial activity precisely under the conditions that normally exist in inflammatory areas; hence it acts as a natural antibiotic. In contrast to lactic acid, other substances accumulating at the site of a necrotic breakdown, such as keto acids, favor bacterial growth under the very same conditions and can antagonize to some extent the bactericidal effect of lactic acid. Suggested evidence of this relationship is found in the great susceptibility to infection associated with uncontrolled diabetes or with acute starvation, in both of which instances ketosis is often present. In both instances, the ensuing infections are easily controlled if the diabetic receives adequate insulin or the starving individual is returned to a satisfactory nutritional state. Hormones, in their turn, can indirectly bring about profound changes in the physiochemical characteristics of the in vivo environment. Thus, cortisone, by reducing the inflammatory reaction, is likely to decrease the production of lactic acid at the site of a lesion. Hence, it appears that susceptibility to infection is an expression of a reversible disturbance, probably biochemical in nature.

Give the various routes by which infection spreads.

In general, there are two possible routes by which infection spreads: (1) contiguous, by direct extension over a large area of a single type of tissue or by penetrating layers of connective tissue that ordinarily would impose a formidable barrier, and (2) hematogenous, by way of the lymphatics, veins, or arterial tree. Certain organisms are enabled to spread through tissue by the elaboration of an enzyme, hyaluronidase, which breaks down hyaluronic acid, a component of the ground substance of connective tissue. This bacterial enzyme is apparently identical with that recovered from animal tissues, such as testes, where it is a main component of the "spreading factor."

Does fever always indicate that a disease is infectious?

Although fever is usually present in infectious diseases, it does not follow that fever always indicates that the disease process is infectious. Interference with evaporation of moisture on the skin by high humidity of the air, or lack of sweating due to congenital epithelial defects such as ichthyosis may raise the body temperature. Fever may result from hemorrhage into tissue, malignancy, disturbances in the hypothalamus, psychic disturbances, excessive muscular fatigue, and other causes.

What factors influence the total white blood count in infectious diseases?

Since different organisms have different chemotactic powers, there is a variance in mobilization of leukocytes. The pneumococcus usually induces a striking leukocytosis (15,000 to 25,000 per cubic millimeter of blood), whereas in typhoid fever the total white count is low or normal. In some diseases, such as those due to viruses, malarial parasites, etc., the causative agent is immobilized in cells within the bone marrow so that a low peripheral count (leukopenia) results. Usually, a drop in white-cell count in the course of a disease in which leukocytosis ordinarily occurs is indicative of a poor prognosis, whereas the appearance of a leukocytosis in a disease in which the count is low or normal usually heralds a complication.

Discuss the mechanism of chills which accompany acute infections.

After the blood stream is invaded by the offending infectious agents, a foreign protein is liberated; the antigen-antibody reaction which results is usually accompanied by constriction of the peripheral arterioles of the host. The diminution in blood flow to the skin causes local chilling and the resultant shivering or shaking represents a reflex increase in muscular activity that raises the internal temperature in an attempt to compensate for the lowered skin temperature.

Is there any basis for the clinical observation that poliomyelitis frequently attacks the most well-nourished and apparently healthy children?

Studies on viruses suggest that these organisms must depend on the host cells for some respiratory enzymes necessary for growth and reproduction. Hence, a high level of nutrition and vitamin storage may increase the susceptibility to poliomyelitis; this hypothesis is directly the opposite of that generally held true with regard to bacterial infection.

Give several examples of the tissue adaptability of the infecting agent.

Some infectious agents apparently prefer certain types of tissue. The gonococcus has a predilection for the mucous membrane of the lower urinary tract, the genital organs, or conjunctiva; the tubercle bacillus settles in the lymphoid tissue; the virus of yellow fever appears to prefer hepatic cells.

Discuss the role played by rest in bed in the management of infectious diseases.

Rest in bed represents the first therapeutic measure which an infected person should apply to himself. Not only does the recumbent position lessen malaise and relieve the sense of fatigue, but the work of the heart, kidneys, and liver is reduced. Blood flow to the kidneys and liver tends to be greater in the recumbent position. However, bed rest has certain disadvantages, namely diminished respiratory excursions, which may lead to atelectasis, and a sluggish blood flow, which predisposes to phlebothrombosis in the lower extremities. Furthermore, prolonged confinement may have an unfavorable psychological effect on the patient.

Discuss the value of the differential white blood count as an index of the progress of an infection.

Alterations in the polymorphonuclear leukocytes may be caused by certain toxins; for example, leukocidin, a soluble exotoxin elaborated by the hemolytic *Staphylococcus aureus* affects the mature cells more than the immature leukocytes, so that the segmented forms are progressively replaced by stab forms, juveniles, and myelocytes. Since the production of cells in the bone marrow is not depressed, the total count may be unaltered, but the Schilling hemogram shifts to the left and toxic granules appear. As the antitoxin titer increases, the leukocidin becomes inactivated, and the total white-cell count rises, with an accumulation of more mature neutrophils. Likewise, the rise in the eosinophil count during the course of an infection reflects the beginning of recovery and denotes a good prognosis. However, eosinophilia occurs with parasitic infections and with allergic states. In the former, the eosinophilic response reflects both a chemotactic effect on blood cells and an allergic response. Finally, the total lymphocyte and monocyte counts at times reflect the progress of the underlying pathological processes. The prognosis of tuberculosis may be estimated by the proportion of large mononuclear cells and small lymphocytes in the blood, in that the former, after leaving the peripheral blood, phagocytize tubercle bacilli and form the multinucleated Langhans type of giant cells and also have the ability to transform themselves into epitheloid cells, which help to wall off the bacillus in the tubercle. The lymphocytes appear as the tubercle is more fully formed and later form a surrounding collar at the periphery. Hence, when the number of large mononuclear cells exceeds the number of small lymphocytes in the blood, one may predict the spread of the tuberculous process, with the formation of new tubercles. Conversely, one may predict a decrease in new tubercles and a more effective seal-off by the lymphocytes of those already present.

What are some of the indirect or long-term effects of an acute infection?

Usually, the damage that accompanies or immediately follows an acute infection is readily recognized, whereas the long-term effects are frequently not fully appreciated. For example, rheumatic fever may produce an acute myocarditis which is easily recognized and handled successfully, whereas an acute valvulitis occurs more frequently but with less dramatic and immediate symptoms, only to persist and cause scarring and distortion of the valves, which ultimately leads to an interference of blood flow through the heart, the usual cause of death in rheumatic fever. Furthermore, the disease process may be reactivated by an acute infection elsewhere in the body—usually in the upper respiratory tract and due to the beta hemolytic streptococcus—by virtue of the antigen-antibody mechanism concerned with the production of rheumatic lesions. Similarly, lesions suggesting those of periarteritis nodosa have been reproduced experimentally in animals by the administration of sulfonamides, suggesting an antigen-antibody reaction mechanism. Repeated attacks of pulmonary infections give rise to secondary changes in the lungs, i.e., chronic pulmonary disease, which eventually interferes with the transmission of oxygen across the capillary bed of the lung, with resulting chronic anoxia.

What role do circulating antibodies play in the recovery from an infectious disease?

Recovery from an infection is dependent upon immunity (specific factors) and resistance (nonspecific factors). Most immunity that develops during natural recovery from a disease is due to a mixture of circulating (humoral) and fixed (cellular) antibodies. The antibodies begin to appear in the circulating blood after 5 to 10 days of an initial infection and the antibody is usually a globulin, which is a relatively large protein molecule. The size of the antibody is important in the mechanism of recovery, since a gamma-globulin is less likely to pass cell membranes than is a smaller protein molecule and hence cannot reach organisms growing intracellularly. Antibodies are formed against specific substances which have a protein in the molecule, and the protein fraction of the bacterial body usually leads to the production of agglutinins that alter the physical characteristics of the bacterial cell wall, so that it adheres more readily to adjacent organisms. The resultant clumping of the bacteria facilitates mechanical removal of organisms from the blood stream by phagocytosis. Frequently, these circulating antibodies cannot act on bacteria unless complement—a fraction of normal blood serum—is also present. Furthermore, the agglutinins cannot penetrate encapsulated organisms in order to produce agglutination.

Why is a high protein intake of importance in the supportive therapy of infectious diseases?

The excretion of nitrogen in the urine is often increased during an infectious illness, as a result of either a high rate of protein destruction, which may represent an effort to produce more calories, or some specific chemical change concerned with the breakdown of preformed body tissues. Furthermore, protein may be lost from the circulating blood into the interstitial spaces; at times, this loss may act as a precipitating factor in the development of peripheral circulatory collapse. Hence, the great importance of sufficient protein intake to maintain nitrogen balance in a given infection. This is best obtained by supplementary feedings of food, rather than by amino acids or protein hydrolysates or by attempting to maintain protein balance by the intravenous administration of preformed protein (plasma, albumin, or blood).

By what methods may the natural course of an infection be altered?

The natural course of an infection may be altered by preventive and therapeutic measures. Preventive methods include attempts at the control of the environment, such as public health measures directed at the eradication of reservoirs of infection, control of anthropod vectors, isolation of infected persons, etc.; active and passive immunization against specific infections; and chemoprophylaxis in selected instances. Therapeutic measures directed toward inhibiting the growth and reproduction of the offending organism until the immune mechanisms of the body are able to ensure recovery include the various antimicrobial agents—the synthetic drugs (sulfonamides, isoniazid, para-amino salicylic acid, etc.), antibiotics, antisera, antitoxins, and others.

Discuss the factors involved in the effectiveness of antimicrobial therapy.

(1) The susceptibility of the etiological agent, or agents, to the various drugs; (2) the ability of the drug to reach the pathological process in adequate concentration; (3) the toxic reactions associated with the use of the drug; (4) the presence of substances that may be elaborated by the organism (penicillinase) or by the host (tissue breakdown products, pus, etc.) that inhibit the action of the drug; (5) the development of drug resistance in an organism previously susceptible to the agent; and (6) the degree of immunity in the host.

Define the term "allergy."

This word has been applied to a large and varied group of conditions in which the tissues or organs of one person respond to contact with some foreign material in a definitely different manner from the corresponding tissues or organs of other persons. The phenomena of allergy are highly specific, and the degree of specificity corresponds to that characteristic of reactions between antigen and antibodies. The term "allergy" is intended to include those reactions mediated by an antibody, or in which such a mechanism appears probable, while excluding other idiosyncrasies in which entirely different mechanisms are involved.

What is the basic pathologic lesion in asthma, allergic rhinitis, urticaria, and angioedema?

A local vasodilation and increased capillary permeability leading to tissue edema in the bronchial or nasal mucosa or in the skin and subcutaneous tissue. In asthma and rhinitis there is an increase in mucoid secretion, and in asthma there may be also associated spasm of the smooth muscle of the bronchial walls.

Give several examples of the relationship between allergy and infectious diseases.

Among individuals who are predisposed to sensitization by heredity, there are many with allergic disorders (asthma, urticaria, rhinitis, etc.) in whom no demonstrable external allergen is present, but, after the eradication of infection within the body, the allergic symptoms are relieved. Likewise, the reproduction of symptoms occurs when an overdose of an autogenous vaccine is injected. In addition, it is well recognized that previous contact with an infectious agent might greatly change the response to a fresh exposure, not only by the development of immunity, but also by an altered reaction as in tuberculosis (tuberculin sensitivity). Sensitivities of the tuberculin type are developed in a wide variety of infections—typhoid fever, brucellosis, coccidioidomycosis, etc. In addition, the anaphylactic type of sensitization to infective agents is observed in certain metazoal parasitic diseases caused by filaria, ascaris, echinococcus, etc. Finally, there is much evidence that rheumatic fever is caused by sensitization to certain strains of streptococcus and, although the exact mechanism is not known, the demonstration of antistreptolysins in the blood is of diagnostic value. Bacterial sensitization may also play a role in the pathogenesis of erysipelas, scarlet fever, periarteritis nodosa, and lupus erythematosis.

What mechanisms are involved in drug allergies?

Except for biological drugs containing protein, most drugs are not antigenic in the true sense of inducing antibody formation if injected into experimental animals. Nonantigenic agents, such as penicillin, combine with the body proteins to form complex antigen, the specificity of which is determined by the nonantigenic foreign substance. This hypothesis is the basis of the hapten theory, which is accepted by many as the explanation of allergy to penicillin and other nonantigenic substances. However, other workers are of the opinion that penicillin, as such, does not combine with protein and is not the antigen that produces penicillin allergy; rather that penicillanic acid is the offending agent. Thus, the diagnosis of drug allergy is often difficult, since the skin tests that are valuable in other forms of allergy, except for patch tests in contact dermatitis, are not reliable as evidence for nonprotein drugs. Likewise, it is impossible as a rule to demonstrate the presence of skin-sensitizing or other antibodies in the serum.

Discuss the use of corticotropin and the cortisone drugs in allergic reactions.

The beneficial effects of corticotropin and the cortisone drugs have been observed in a wide variety of allergic reactions, including the immediate-wheal skin-reacting type (hay fever, asthma, urticaria, etc.), in dermatitis, asthma, and rhinitis due to bacterial allergy, and in a group of allergies not manifested by the wheal reaction on skin test. Thus far, the mechanism of action of these hormones is not understood.

Section 4

PHARMACOLOGY

TERMINOLOGY

Define pharmacology.

Pharmacology is the science of drugs. It embraces the description of:

(*a*) *Pharmacy:* the collection, preparation, and standardization of drugs.

(*b*) *Pharmacognosy:* the identification of drugs.

(*c*) *Materia medica:* description and preparation of drugs.

(*d*) *Toxicology:* the effects of poisons and noxious effects of drugs.

(*e*) *Pharmacodynamics:* the response of normal organisms to drugs.

(*f*) *Pharmacotherapeutics:* the reactions of diseased organisms to drugs.

What are pharmacodynamic agents?

Substances which by virtue of a physical or biochemical action alter the physiological activity of cells, organs, or organisms by stimulation, depression, or irritation.

What are chemotherapeutic agents?

Substances which possess toxic actions on bacteria and other parasitic invaders of the body without serious toxic or pharmacodynamic effects on the recipient.

Define antagonism.

When two drugs have opposite action on the same organ or system of organs, the presence of both agents will result in antagonism.

Define synergism.

The reaction of two or more drugs used concomitantly to produce a response that is more effective than that which a single drug, or agent, produces. It may be characterized as *summation* when the effects are simply additive, or as *potentiation* when the combined action is greater than the sum of their individual actions.

Define cumulative action.

When drug activity is characterized by a slower rate of inactivation or elimination that that of administration, the summation of action of successive doses is known as the cumulative effect.

Define tolerance.

Resistance or insensitivity to drug action at usual dosage levels. It may be congenital or acquired.

Define idiosyncrasy.

A response to a drug that is excessive or different from the usually observed pharmacological action.

CLASSIFICATION AND NATURE OF DRUGS

What are mineral drugs?

Elementary substances, free acids, and metallic hydroxides, as well as the salts of acids, have been employed for pharmacological and therapeutic actions; examples of each include sulfur, hydrochloric acid, aluminum hydroxide, and magnesium sulfate.

What are animal drugs?

Pharmacologically active substances that have been obtained from organs of animals are known as animal drugs. Their use has included substitution therapy as well as pharmacotherapeutic actions. Examples are insulin, which is a crystalline preparation of pancreatic extract, and the adrenocorticotropic hormone, which has been obtained as an extract of the pituitary gland.

What are vegetable drugs?

Substances of pharmacological activity that are obtained from plants are known as vegetable drugs. Although plants once served as valuable sources of many drugs, the laboratory and the biological chemist have succeeded in identifying the active chemical constituents of these pharmacological agents and have succeeded in many instances in synthesizing or improving these agents by chemical alterations. Vegetable drugs are classified as alkaloids, glycosides, oils, resins, and gums.

Define alkaloids.

Alkaloids are nitrogenous organic substances of basic reaction that possess an amine structure; they may be either of plant or animal origin. They are the chief constituents of active principles of vegetable drugs and are identified by the English suffix *-ine*. Atropine is the principal alkaloid of the plant belladonna. Epinephrine is the active principle of the medullary portion of the adrenal glands.

For what reason are the salts of alkaloids used instead of the basic alkaloids?

The salts of alkaloids are freely soluble in water, while the basic alkaloids are practically insoluble.

Define glycosides.

Glycosides are organic substances that combine sugars in an ether-like linkage with other organic structures, such as alcohols, aldehydes, and phenols. They are recognized in English terminology by the suffix *-in*. When the sugar in such a linkage is glucose, the compound is referred to as a glucoside. Glycosides may be split by the action of a dilute acid or by fermentation reaction into the sugar and the residual structure, which is known as an "aglycone" or "genin." An important example is the group of cardiotonic glycosides, which include substances such as digitoxin, gitalin, and cedilanid.

Define vegetable oils.

Vegetable oils are hydrocarbons obtained from plants; they may be classified as fixed and volatile oils. Fixed oils include the glycerides of oleate, palmitic, and stearic acids, which are chiefly useful as vehicles or as ingestants with high caloric value. Volatile oils are characterized by the physical property of being volatilized by heat; their chief use at present is as flavoring agents. They have been used in the past for their carminative, irritant, or analgesic action.

Define tincture, extract, and ointment.

Tincture: A solution in alcohol or aromatic spirits of ammonia of a nonvolatile substance (exception: tincture of iodine).

Extract: A solid or semisolid preparation made by evaporating a solution of the active constituents of vegetable drugs to the required consistency.

Ointment: A fatty preparation, soft or solid at ordinary temperatures, with a base of petroleum, lanolin, lard, olive oil, or other unctuous substance.

What is the ordinary relative strength of a tincture to a fluidextract of the same drug?

Tinctures vary in strength from 5 to 50 per cent, the majority being 10 per cent. In fluidextracts 1 cc. is equivalent to 1 gm. of the drug extracted; hence fluidextracts are on the average 10 times as strong as tinctures.

Define spirits.

Alcoholic solutions of volatile substances. Fourteen are solutions of volatile oils.

What are the determinants of drug dosage?

(*a*) Age, (*b*) body weight, (*c*) individual reactivity, (*d*) the route of administration, (*e*) rate and ability of absorption by host, (*f*) the manner and rate of distribution, (*g*) the mode of inactivation or elimination.

Name and describe the methods of administering medications.

(*a*) *Oral:* The drug, either solid or liquid, is swallowed and absorbed in the stomach and small intestine.

(*b*) *Rectal:* The drug can be administered in liquid or semisolid form for absorption in the large intestine. Enemas or suppositories are the usual forms. The rectal dose should be roughly about double that given by mouth for most agents but somewhat less for narcotics.

(*c*) *Hypodermic:* The drug, in solution in sterile water, salt solution, or oil, is injected with a hypodermic needle into the subcutaneous tissue, or more deeply into the muscular tissue of the buttocks, arm, thigh, or abdomen. Protective or immunological sera, as well as those possessing curative value, may be administered in the same fashion. Hypodermic doses should generally be less than those given by mouth.

(*d*) *Epidermic or Inunction:* After thorough cleansing of the skin with soap and water and alcohol, an ointment containing an active drug or penetrating substances is rubbed onto the skin.

(*e*) *Iontophoretic:* The active drug, in solution, is in contact with the skin under a suitable electrode. An electric current is then employed to cause migration of the active drug through the intact skin into the subcutaneous areas where it is picked up by the circulation.

(*f*) *Inhalation:* Volatile drugs and gaseous agents are rapidly absorbed by the respiratory mucous membranes. The vapor of water may also be medicated with the drug and inhaled, usually for local effects.

(*g*) *Intranasal:* Absorption by the nasal mucous membranes can be used for local or systemic effects.

(*h*) *Sublingual:* Solid drugs may be absorbed locally by the mucous membranes of the mouth when placed under the tongue.

(*i*) *Intravenous:* In cases of emergency when rapid action is desired, this route is used for the introduction of parental fluids and for other drugs that cannot be injected into the subcutaneous tissues.

(*j*) *Intramarrow Injections:* These are employed for rapid injection into the circulation when the use of intravenous therapy is impractical, such as in the administration of fluid, blood, or other medications to small infants, or in adults when superficial veins are no longer available or accessible because of severe tissue destruction.

PARENTERAL FLUID THERAPY

State the purpose of parenteral fluid therapy.

Parenteral fluid therapy is employed to replace losses and to maintain the daily requirements of fluids, electrolytes, calories, amino acids, and vitamins in cases in which oral administration is impossible or impractical. The intravenous route is usually reserved for patients with severe dehydration, acid-base imbalance, etc., whereas those with mild dehydration may be treated with isotonic solutions subcutaneously. The problems associated with subcutaneous fluid therapy (uncertain absorption, discomfort to the patient, and limited quantities of administration) are somewhat alleviated by the use of hyaluronidase preparations (Hyazyme, Diffusin, Wydase).

Give the contraindications for the use of hyaluronidase.

Hyaluronidase should not be injected into areas of active infection or malignant disease.

Give the average daily water requirement for man.

The average adult water requirement is 2,000 to 3,000 ml. per day: 1,000 to 1,500 ml. for loss through insensible perspiration from lungs and skin, and 1,000 to 1,500 ml. for urinary excretion. Patients with fever and sweating require additional amounts of 500 to 1,000 ml. during the day.

Give the advantages of carbohydrate solutions for intravenous administration of fluids.

Carbohydrates, in the form of glucose, fructose, or alcohol are added to water to make the solution isotonic and thus prevent hemolysis of the red blood cells within the vascular tree and to institute a series of measures that overcome abnormal metabolic reactions. Although the use of carbohydrates in water does not serve to give the body the necessary electrolytes, they can be used as a source of calories in either isomolar solutions or those up to 25 per cent. They must be administered slowly or glycosuria will occur, with renal spilling. In high concentrations, they are irritant and sclerosing to blood vessels.

List several purposes served by the administration of carbohydrate solutions.

(1) They provide water to supply the body needs for insensible perspiration and urine output. The water is supplied by both the oxidation of carbohydrate and water per se. (2) They supply calories for the daily metabolic needs, especially for protein synthesis. (3) They prevent and/or stop the production by the liver of excess ketones due to depletion of liver glycogen. (4) They spare the excessive loss of nitrogen due to breakdown of tissue protoplasm of the body. (5) They spare the loss of intracellular water. (6) They conserve the intracellular electrolytes, e.g., potassium, and spare the loss of extracellular electrolytes, e.g., sodium. (7) They decrease the amount of water necessary for kidney excretion by decreasing the load of ketone bodies, nitrogenous products, and electrolytes that have to be excreted by the kidneys.

In addition to water and carbohydrate, what other requirements are necessary in patients treated with parenteral fluids?

If a patient requires parenteral fluids for more than 48 hours, it is obvious that the quantity of calories supplied by carbohydrates alone is not sufficient to satisfy the daily requirements. Therefore, the patient should be given proteins in the form of an amino acid solution (protein hydrolysates, enzyme digests, etc.). A minimum of 40 gm. per day should cover the basic needs of the body; this is supplied by administering 1,000 ml. of a 5 per cent amino acid solution. In addition, potassium, magnesium, and calories from carbohydrates are required for the proper deposition of nitrogen as protein. Likewise, for the proper intermediary metabolism of carbohydrates, it is necessary to administer vitamins (B complex and C).

State the minimal daily requirements of sodium, chloride, and potassium.

The exact minimal daily requirement in man of sodium, chloride, and potassium are not known. However, the daily requirements will be satisfied by: for sodium, 100 mEq. contained in approximately 6 gm. of sodium chloride; for chloride, 120 mEq. contained in 7 gm. of sodium chloride; and for potassium, 60 mEq. contained in 4.5 gm. of potassium chloride.

What is isotonic saline solution?

Isotonic saline solution contains 154 mEq. of sodium per liter and 154 mEq. of chloride per liter of solution and is therefore not normal saline, since the blood level of sodium is 142 mEq. per liter and of chloride 103 mEq. per liter. Hence, the so-called normal, or physiological, saline should not be referred to as isotonic saline solution.

What is the most appropriate solution for routine intravenous use?

Ringer's-lactate solution, which contains in each liter: sodium (130 mEq.), chloride (111 mEq.), potassium (4 mEq.), calcium (4 mEq.), and lactate (27 mEq.). As indicated, in addition to sodium and chloride, it contains potassium and calcium, which serve to prevent a dilution of these electrolytes in the blood, and lactate, which, under normal conditions, is oxidized or built into glucose and glycogen.

Differentiate between hypertonicity and hypotonicity.

The blood is considered hypertonic if the plasma or serum sodium is elevated above 142 mEq. per 1,000 ml. It is hypotonic if the sodium value is below 142 mEq. per 1,000 ml. Hypertonicity occurs in pure water dehydration or in a mixed dehydration, in which more water is lost than salt. Treatment consists of administering water and carbohydrate. Hypotonicity results from giving large amounts of fluid without electrolytes and from various conditions leading to the "low salt syndrome." Treatment consists of the cautious use of hypertonic saline intravenously and the restriction of water by mouth.

What functions do the colloid solutions serve in parenteral fluid therapy?

The various colloid solutions include whole blood plasma, human serum albumin, and plasma expanders such as dextran, polyvinylpyrrolidone (PVP), and gelatin. These solutions are employed to prevent shock, to support the circulation, and to supply additional proteins to aid the plasma osmotic pressure.

What is the chief danger of using normal human plasma?

The transmission of homologous serum hepatitis. In addition, it is to be remembered that sodium chloride is present in human plasma; plasma prepared from outdated bank blood will have a high potassium concentration.

Outline the maintenance of daily requirements for short-term, long-term, and postoperative parenteral fluid therapy.

Regardless of the length of time that parenteral fluids are administered, it is important that accurate accounts of fluid intake and output, including measurements of abnormal loss of secretions (vomitus, drainage, etc.) are recorded; the general state of the patient must be evaluated as to hypotension, hemoconcentration, oliguria, azotemia, cardiac function, diabetes, etc.; and frequent determinations of essential electrolytes are indicated. For short-term (24 to 48 hours) parenteral fluid therapy, a minimum of 2,000 ml. of fluid per day will prove satisfactory. Included in this amount are 1,500 ml. of 10 per cent carbohydrate and 500 ml. of Ringer's-lactate in 5 per cent carbohydrate. For long-term (over 72 hours) maintenance, the patient should receive a minimum of 2,500 ml. of fluid per day. This includes 1,000 ml. of 5 per cent amino acids in 10 per cent carbohydrate, 500 ml. of Ringer's-lactate in 5 per cent carbohydrate, 3 gm. of potassium chloride in 1,000 ml. of 10 per cent carbohydrate solution, and vitamins B (complex) and C.

The daily maintenance of surgical patients is obviously complicated by various factors, such as surgical insult to tissues, etc. In general, at the time of operation the patient is given 500 ml. of hypotonic saline, and, if indicated, whole blood; this is followed with 1,500 ml. of 10 per cent carbohydrate solution. Since surgery often results in loss of potassium and a negative nitrogen balance, the patient, after the first 24-hour period following operation, is given the routine outline for long-term parenteral therapy.

Give the solution of choice for the treatment of acid-base imbalances.

For metabolic acidosis (low pH and and low carbon dioxide capacity) the solution of choice is Ringer's-lactate. For severe cases with hyperpnea (Kussmaul respiration) ⅙ molar sodium lactate should be used. In patients with metabolic alkalosis (high pH and high carbon dioxide capacity) and respiratory alkalosis (high pH and low carbon dioxide capacity) the solution of choice is Ringer's, which contains in each liter: sodium 147 mEq., chloride 155 mEq., potassium 4 mEq., and calcium 4.5 mEq. For severe cases of metabolic alkalosis, ammonium chloride gastric solution may be tried; and, if tetany occurs in instances of respiratory alkalosis, calcium gluconate or calcium chloride is given intravenously. In respiratory acidosis (low pH and high carbon dioxide capacity), the dehydration is treated with hypotonic saline and carbohydrates. In severe cases, Ringer's-lactate should be administered.

Give the causes of potassium intoxication.

Usually, potassium intoxication results from a too rapid intravenous infusion of potassium salts or an extreme degree of renal insufficiency; in addition, abnormally high potassium concentrations occur in the body with adrenal insufficiency. A diagnosis of potassium intoxication is dependent upon a plasma-level determination. In patients requiring massive, multiple transfusions this is indicated, especially if the blood has been stored for more than one week, since such blood has a very high potassium concentration. Although a presumptive diagnosis of potassium intoxication may be made on the basis of characteristic change in the electrocardiogram, the diagnosis is dependent upon a plasma-level determination of potassium.

PRESCRIPTION WRITING

Define prescription.

A prescription is the physician's order to the pharmacist with directions as to preparation of the prescribed drugs by the pharmicist and their use by the patient.

Why is prescription writing rapidly becoming a lost art in medicine?

(1) The complicated and often useless mixtures of yesteryear have been replaced by single, or combinations of several, effective drugs.

(2) The more useful mixtures are included among the official preparations of the Pharmacopoeia or National Formulary and may be ordered simply by reference to these publications. (3) The pharmaceutical industry has made drugs in forms suitable for their most convenient administration. (4) The annual Physician's Desk Reference (PDR), New and Nonofficial Drugs, Merck Index, American Drug Index, and U.S. Dispensatory assist the physician in keeping pace with the rapid progress in pharmaceutical specialties and biologicals. (5) The physician today need no longer rely on the obscurantism of Latin to make a pretense of learning, and also the increasing medical intelligence of the laity allows a type of cooperation between patient and physician in which secrecy has no part.

What ingredients does a traditional inscription include?

The inscription, or body of the prescription in which the prescribed drugs are listed, includes: (1) the basis, or principal drug; (2) the adjuvant or secondary drug, which may add to the effectiveness of the basis; (3) the corrective, to overcome any undesired effects of the active principles; and (4) a vehicle or excipient in which the preceding are incorporated and rendered palatable. However, today, only rarely do prescriptions include all four types of ingredients. Instead, most prescriptions consist of a single constituent and, if a mixture is employed, one can advantageously prescribe the official prescription.

What is incompatibility in medicine, and what are the different kinds of incompatibles?

When two or more drugs are incorporated into a single medication and when these substances react in a manner to produce an effect not originally intended or desired by the physician, such substances are defined as incompatibles. Drugs may be chemically, physically, pharmaceutically, or therapeutically incompatible.

(*a*) *Chemical incompatibility* occurs when substances precipitate each other in solution, form explosive compounds or volatile ingredients, or when chemical decomposition takes place; example—the liberation of carbon dioxide when carbonates are mixed with acids. (*b*) *Physical incompatibility* occurs when precipitates are formed that have a chemical action usually resulting in an unsightly mixture, or when solid substances undergo liquefaction or deliquescence; example—the precipitation of salts of alkaloids in strongly alcoholic solutions. (*c*) *Pharmaceutical incompatibility* occurs when the ingredients produce an unpleasant-tasting or appearing substance; example—the formation of soaps when alkalis are mixed with fixed oils. (*d*) *Therapeutic incompatibility* results when two antagonistic drugs are incorporated in a given prescription; example—a preparation containing physostigmine and atropine.

What error does this prescription demonstrate?

Name G. W. Smith
January 2, 1962
Doeville

℞	Potassium iodide	8	0
	Strychnine sulfate		03
	Ferrous sulfate	4	
	Simple syrup	30	
	Water to make	90	
	Mix well in solution		

Sig. One teaspoonful three times
a day after meals.
Dr. T. L. JONES

Potassium iodide is incompatible with the alkaloid and also with the metal salt.

Name two drugs incompatible with hyoscyamus.

The incompatibles of hyoscyamus are the same as those of belladonna—the caustic alkalis and vegetable infusions containing tannic acid.

The dose of a medicine given by mouth being 1 grain, what would be the equivalent does for hypodermic use and what for administration by rectum?

No definite rules can be given, as the absorbability of different drugs varies within wide limits. Roughly, the dose for hypodermic injection should be about three fourths the dose by mouth, and the rectal dose twice as large. Opium is absorbed almost as completely when given by the rectum as when administered by mouth.

By what rule would you determine the dose of any medicine for a child?

Divide the age by the age + 12; the resulting fraction represents the proportion of the adult dose. For example, the dose for a child of 3 years is $3 \div (3 + 12) = 3/15$ or $1/5$ of the adult dose.

However, in most instances the ratio of the weight of the child to 150 (adult weight) is used.

What are the standard units of the metric system of weights and measures?

(1) The *meter*, the unit of length, is equal to $1/40$ of a millionth part of the

earth's circumference; (2) the *liter,* or unit of capacity, equal to the cube of 1⁄10 of a meter or a cubic decimeter. (3) The *gram,* unit of weight, is equal to the weight of 1 cc. of water at 4°C.

In prescription writing the following units and subdivisions are used: the *gram* (*gm.*), equivalent to 15 or 16 grains (15.432); the *cubic centimeter* (*cc.*), equivalent to the same number of minims. Centigram (cg.) and milligram (mg.) are seldom used, the quantities being expressed in decimal fractions of a gram; thus, 2 cg. = 0.02 gm.; 3 mg. = 0.003 gm., etc. The symbols gm. and cc. are not written as a rule. A vertical line at the right of the prescription blank separates the grams or cubic centimeters from fractional quantities, thus taking the place of a decimal point.

1 gm. or cc. = 15 grains or minims.
4 gm. or cc. = 1 dram or fluidram.
30 gm. or cc. = 1 ounce or fluidounce.
500 gm. or cc. = 1 pint (Oj).

Write the following prescription in the metric system:

℞	Strychninae sulfatis,	gr. ss;
	Acidi hydrochlorici diluti,	f℥ ss;
	Tincturae cardamomi,	f℥ ij;
	Tincturae gentianae compositae,	q.s. ad f℥ iij.—M.
Sig.	One teaspoonful three times a day before meals.	

℞	Strychninae sulfatis,		03
	Acidi hydrochlorici diluti,	15	
	Tincturae cardamomi,	8	
	Tincturae gentianae compositae,	q.s. ad 100	M.
Sig.	One teaspoonful three times a day before meals.		

Which drugs may be refilled on the patient's order without the physician's approval?

Only prescriptions for nondangerous drugs may be refilled without the physician's approval, as the Durham-Humphrey amendment to the Federal Food and Drug Act prohibits the pharmacist from refilling other prescriptions unless the physician has stated on the original prescription that subsequent refills are permitted.

What must be included on a prescription for narcotics?

The physician's Federal Narcotic License number, the physician's name, address, and signature in ink, the patient's name and address, and the date. It is also an excellent custom for the physician to keep an exact, or carbon, copy for his files.

TOXICOLOGY

What is a poison?

Any substance applied to the body, ingested, inhaled, or developed within the body, which causes or may cause damage or disturbance of function.

Give an example of (a) irritant, (b) narcotic, and (c) narcotico-irritant poisons.

(*a*) *Arsenic,* from mineral; *gamboge,* from vegetable; *cantharides,* from animal.

(*b*) Opium and hydrocyanic acid.

(*c*) Strychnine.

What is the difference between an antagonist and antidote?

Antagonists are drugs that are opposed to each other in their physiological effects and pharmacological activity. Antidotes are agents that are administered for the purpose of counteracting the action of a poison. Antidotes are divided into three general classes: (*a*) *Chemical*—The nature of the poison is chemically changed so that it becomes insoluble or harmless. Chemical antidotes are chiefly useful for their action in the stomach where they precipitate or chemically unite with drugs to render them harmless or prevent absorption. (*b*) *Mechanical*—Mechanical antidotes prevent absorption of the poison by holding it in a physical suspension or by coating the stomach. (*c*) *Physiological*—

Antidotes which in general antagonize the poison physiologically; for example, the use of central motor system stimulants in barbiturate poisoning.

Mention the antagonists of cocaine.

Morphine, chloral, amyl nitrite, alcohol, chloroform, and ether.

What drug is antagonistic to pilocarpine?

Atropine sulfate is directly opposite in action; $\frac{1}{100}$ grain neutralizes the effect of $\frac{1}{6}$ grain of pilocarpine.

By which routes may chemicals enter the body?

(1) Inhalation of chemicals by the lungs, which offers the greatest risk of injury because the lungs provide the greatest surface of contact and the weakest barrier to absorption. In addition, entry into the blood stream of the lungs provides the shortest route to the heart and the brain and eliminates the chemical detoxifying function of the liver before recirculation occurs. (2) Absorption through the skin or mucous membranes. (3) Absorption by the gastrointestinal tract.

Classify the symptoms associated with toxic chemical agents.

(1) Symptoms arising from irritation and damage at the site of entrance—bichloride of mercury on the stomach, acids on the skin, lye on the esophagus, nitrous gases on the respiratory tract, etc. (2) Symptoms arising from action at the site of excretion—mercury on the colon and kidneys, beta-naphthylamine on the urinary bladder, etc. (3) Symptoms due to selective action of chemicals on metabolic processes, enzyme systems, and other cellular functions—hematopoietic function suppressed by benzol, respiratory tissue affected by cyanide, liver damage by TNT, etc.

Mention the metals whose salts are often taken as poisons.

Arsenic, mercury, antimony, lead, silver, copper, and zinc.

Mention the antidote applicable in a case of poisoning with silver nitrate. How does the antidote act?

Common table salt, *sodium chloride.* It produces insoluble silver chloride, which is nontoxic.

Name the chemical antidotes for poisoning with caustic alkalis.

Fats or oils; vinegar or acetic acid well diluted with water; lemon juice (citric acid).

State the most common and convenient antidotes for poisoning with (*a*) acids, (*b*) alkaloids.

(*a*) *Acids:* Neutralize with milk of magnesia, aluminum hydroxide gel, calcium hydroxide solution, lime water, or wall plaster crushed in water. *No stomach tube or emetic.*

(*b*) *Alkaloids:* May be inactivated by potassium permanganate or tannic acid in solution.

Give a universal antidote to be employed when the nature of the poison is not known.

Powdered charcoal, 2 parts; tannic acid, 1 part; and magnesium oxide, 1 part. Dose: 1 teaspoonful to 1 tablespoonful suspended in water. In an emergency, powdered burnt toast, very strong tea, and milk of magnesia can be used as a substitute.

Define poisoning by methyl alcohol (methanol, wood alcohol).

The ingestion of methanol is followed by delayed toxic reactions characterized by nausea, headache, dyspnea, epigastric pain, cyanosis, impairment of vision, and convulsions. Symptoms may not appear until 12 to 18 hours after drinking methanol. Death or permanent blindness occurs in a high percentage of the cases. Methanol is slowly excreted in the breath and in the urine. The toxic effects are believed to be due to the marked acidosis which occurs when methanol is metabolized; formic acid and formaldehyde are formed during this process. In experimental animals, this metabolism can be blocked by the continuous administration of ethanol. Presumably this overloads the enzymatic system; since ethanol is preferentially metabolized, the methanol is excreted unaltered.

Treatment consists of gastric lavage with large amounts of sodium bicarbonate solution, sodium bicarbonate by mouth, and sodium bicarbonate or sodium lactate solution intravenously. In addition, morphine sulfate as necessary for pain; and artificial respiration manually or by a respirator. Ethyl alcohol (ethanol) in doses of 15 to 60 ml. every 2 to 6 hours has been recommended by some workers.

Why are persons with anemia and increased metabolic rates more susceptible to poisoning from carbon monoxide?

Anemic persons are more susceptible to carbon monoxide because the changes in the tissues of the body that result from exposure to this gas are due to anoxia. Likewise, increased metabolic rates enhance the severity of symptoms. This latter principle is employed for the detection of toxic quantities of carbon monoxide with small animals having high metabolic rates (such as canaries in mines).

Discuss the clinical manifestations of and treatment for carbon monoxide poisoning.

Carbon monoxide, formed by the incomplete combustion of carbon, causes central nervous system depression of any degree from headache and mild confusion to deep coma. Patients with severe anoxia may never fully recover. Stoves, furnaces, and automobile-exhaust fumes are common sources of this lethal gas. Although some cases of carbon monoxide poisoning are accidental, they are usually suicidal. Treatment consists of inhalation of carbon dioxide 5 per cent, oxygen 95 per cent; use of a pulmotor for artificial respiration; stimulants; procaine hydrochloride solution intravenously; and blood transfusions.

Outline the management of cyanide poisoning.

Cyanide poisoning may result from the inhalation of hydrogen cyanide or ingestion of acid or salts. The most common sources are etching fluid, rat poison, metal polish, and the seeds of the apple, peach, plum, and cherry. *Prompt treatment is imperative.* Amyl nitrite inhalations for 20 seconds every 3 minutes; sodium nitrite intravenously, 6 to 10 mg. per kg. of body weight (average 10 ml. of 3 per cent solution), and sodium thiosulfate intravenously, 50 to 200 ml. (10 per cent solution). Since the toxicity of cyanide may be reduced by combination with methemoglobin, as produced by amyl and sodium nitrite, and cyanide is converted into relatively nontoxic thiocyanate by the sodium thiosulfate, it is important to give all three preparations immediately.

Give the usual cause and treatment of naphthalene poisoning.

The ingestion of "moth balls," results in headache, nausea and vomiting, increased perspiration, hemolysis and anemia, hematuria or hemoglobinuria, and renal or lower nephron damage. Treatment consists of gastric lavage or emetics, followed by demulcents, stimulants, and intravenous infusions to promote diuresis; blood transfusions may be necessary to combat severe anemia.

Give the mechanism of development and treatment of lead poisoning (plumbism).

Usually, lead poisoning is a chronic disease, resulting from exposure to lead over a relatively long period of time. Absorption of lead can take place from all portions of the respiratory tract (inhalation of lead dusts or fumes), from the gastrointestinal tract (paint, toys, piping), subcutaneously or intramuscularly (shot or bullets), or through the intact skin (tetraethyl lead) or abraded skin (paint, etc.). After absorption into the body, lead is transported to various soft tissues but is soon deposited in bone and slowly leaves the skeleton to be eventually excreted by the bowel and kidney. However, the greatest portion of fecal lead represents unabsorbed lead; the rate of urinary excretion of lead is related to the intensity of exposure and to the blood level. Since the rate of excretion of lead is limited, an excessive exposure results in a positive lead balance, which causes the concentration of lead to increase in all parts of the body; if the exposure is sufficiently prolonged, critical levels will eventually be obtained.

The treatment of lead poisoning is largely dependent upon the control of its distribution and deposition. In this respect, the most important factor is the mechanism by which the body favors the skeletal storage and liberation of lead. Clinical studies have shown that the metabolism of lead is similar to that of calcium and that factors favoring the deposition of calcium in bone would also favor skeletal storage of lead; conversely, decalcification of the skeleton would liberate lead from the bones and permit its excretion. Hence, in the management of plumbism, after the relief of the immediate symptoms with emergency measures—lavage with 1 per cent sodium sulfate solution, catharsis with magnesium sulfate, administration of demulcents such as egg white and milk, relief of colic with intravenous calcium gluconate, and morphine for pain—the patient is given calcium intravenously (5 to 20 cc. of a 5 per cent calcium chloride solution) to remove the lead from the blood and deposit it in the bone. In addition, calcium phosphate (1 to 2 gm.), U.S.P. vitamin D (1 to 2 cc.), and sodium citrate (1 to 2 gm.) are all given orally 3 times daily. After the acute symptoms are controlled, efforts are directed toward preventing recurrence of lead intoxication during the period when the lead content of the body is high and toward shortening the period of convalescence. Obviously, this is dependent upon measures for deleading the skeletal system, which necessitates that the patient be hospitalized and kept in the best possible physical condition. The most effective method of removing lead is the intravenous administration of a solution of calcium disodium versenate (calcium chelate of ethylenediaminetetraacetic acid—EDTA), which combines with lead and promotes its mobilization and excretion. The drug is given by slow intravenous drip (1 gm. in 500 cc. of isotonic sodium chloride solution) twice daily for periods of up to 5 days. If additional treatment is needed, a 2-day rest may be followed by another 5-day course. Other methods of deleading include the administration of a low calcium, high phosphate diet, followed in 3 days by the administration of progressive amounts of ammonium chloride (1 gm.) 3 times daily to a total of 8 gm. daily within a period of a week, and continued until lead is no longer excreted in abnormal amounts. Such therapy should not exceed 3 weeks.

Define phosphoric acid ester insecticides (Parathion, TEPP).

This group of compounds is much more effective than DDT. Parathion, the most widely used, is hydrolyzed only slowly and may remain on fruits or vegetables for weeks. Toxic manifestations have followed the ingestion of such contaminated foods. More commonly, poisoning occurs in those who prepare these products or who use them as sprays. Absorption can occur through the skin, respiratory tract, or gastrointestinal tract. All of these substances are potent inhibitors of cholinesterase enzymes. The symptoms are those attributable to the accumulation of acetylcholine in the tissues; they include nicotine-like, muscarine-like, and central nervous system manifestations. Anorexia or nausea is usually the first symptom; then vomiting, abdominal pain, excessive sweating, and salivation occur. Diarrhea, tenesmus, blurred vision, respiratory difficulties, and pulmonary edema with cyanosis may follow. Muscular fasciculations or weakness may appear; the muscles of respiration may be involved. Central nervous system involvement causes giddiness, anxiety, headache, insomnia, ataxia, tremor, mental confusion, or disorientation. In fatal cases there is coma with Cheyne-Stokes respiration and disappearance of all reflexes. In mild cases, the major symptoms usually subside within a day or two, but weakness may persist for several days. Treatment consists of the following: gastric lavage to remove unabsorbed poison; catharsis, if seen early; atropine sulfate, 2 mg. intramuscularly, repeated hourly until signs of atropinization appear, then repeated at longer intervals, as needed. Artificial respiration, tracheal intubation, or CO_2-O_2 inhalations may be required for respiratory paralysis. Control convulsions with barbiturates or ether. Intravenous fluids as indicated. *AVOID the use of morphine.*

Why is whole milk contraindicated in the treatment of phosphorus poisoning?

Since oil and fatty substances facilitate the absorption of phosphorus, whole milk, cream, and all organic oils and fats are contraindicated in the treatment of phosphorus poisoning. However, nonabsorbable mineral oil accelerates elimination of phosphorus and is indicated after initial therapy, namely, gastric lavage with 0.2 per cent copper sulfate, potassium permanganate solution 1:5,000, hydrogen peroxide solution (2 per cent), isotonic sodium chloride solution, or water. Irrigation is continued until the fluid is clear and then a saline purge is given. Intravenous dextrose solution, protein hydrolysates, methionine, B-complex vitamins, and calcium salts may lessen liver damage.

Discuss the cause and prophylaxis of berylliosis (beryllium poisoning).

Berylliosis, except in accidental massive exposure (to dust, mist, and fumes of the soluble salts of beryllium), represents an allergic disease in which the beryllium ion acts as the sensitizing allergen in both the dermal and pulmonary types of the disease. In view of the lack of specific therapy for berylliosis, certain hygienic prophylactic measures are being employed in plants engaged in ore production of beryllium, namely: (1) devices to control the atmospheric concentration of beryllium, both in the plant and immediate vicinity; (2) screening of new employees, with disqualification on the basis of major allergies (asthma, etc.), history of tuberculosis, major pulmonary infection, chronic cough, malaria, liver or kidney disease, vital capacity below 90 per cent, abnormal cardiac or pulmonary patterns, or inability to wear protective mechanical respiratory devices; (3) instructions to new employees concerning the safety program of the plant; and (4) routine check on all employees, which includes physical examination and chest x-ray every six months, weekly determinations of weight and vital capacity on all potentially exposed persons, care of work clothing, and exclusion from work of all employees with an upper respiratory infection.

Define dimercaprol (BAL).

Dimercaprol, usually called BAL (British anti-lewisite), is used in the treatment of poisoning or untoward reactions from arsenicals, mercurials, and gold salts. These metals exert their action by combining chemically with essential sulfhydryl enzyme systems of the cells. However, BAL is capable of forming complexes with the metals which are then excreted, thereby protecting the enzyme systems of the cells from the inhibiting action of the metals.

List the usual cause and treatment of acute mercury poisoning.

The ingestion of bichloride of mercury. Treatment consists of (1) ingestion of protein material (milk, eggs), (2) copious gastric lavage with a saturated solution of sodium bicarbonate, (3) instillation into the stomach of 6 oz. of a saturated solution of magnesium sulfate before withdrawing tube, and (4) dimercaprol (BAL) 5 mg. per kg.

body weight, intramuscularly, followed in 2 to 4 hours with 2 to 5 mg. per kg., which dose is repeated every 12 hours as necessary.

Give the contraindications for the use of gold in arthritis.

Selected cases of rheumatoid arthritis are benefited by gold therapy, although this form of treatment has not received universal use because of the high incidence of untoward reactions associated with its administration. The most common of these toxic effects are skin reactions, lesions of the mucous membranes (visible, gastrointestinal, and vaginal), blood dyscrasias, and renal damage. Usually, these toxic reactions develop relatively early during the course of gold therapy. Certainly, the high incidence of these untoward effects demands caution when administering gold. The agent should not be used in patients with renal disease, skin disorders, blood dyscrasias, etc., or in the aged.

Give the treatment for rattlesnake bite.

Place a tourniquet 10 cm. above the wound. It should be snug enough to prevent lymphatic drainage, yet not so tight as to prevent arterial and venous flow completely. Wash the area of the bite and make multiple cruciate incisions ½ inch long and ¼ inch deep. Apply suction to the wounds. Continue local treatment for 24 hours with intermittent suction. Tetanus antitoxin or toxoid booster and antibiotics should be given for secondary infection, in addition to general supportive measures where necessary, i.e., blood, oxygen, intravenous fluids, tracheotomy, etc. Whiskey is contraindicated. Specific antivenins should be given immediately. Larger doses are required for children and individuals who have been bitten by large snakes.

What is rabies and how is it treated?

Rabies (hydrophobia) is a spasmodic and paralytic disease due to a virus infection usually transmitted through a wound inoculated by the bite of a rabid animal. *Prophylactic treatment:* When a person is bitten by a supposedly rabid animal and is seen soon after the injury, the wound should be débrided, cleansed with soap and water, and hyperimmune antirabic serum therapy instituted at once. In cases of severe exposure, serum should be given systemically as well as locally. In addition, subcutaneous vaccine (Harris or Semple) is required in the indicated cases of exposure to the bite of rabid animals. If serum has been given, the vaccine inoculations may be delayed for 1 or more days, pending determination of the condition of the biting animal. Depending upon the severity of the exposure, a full (21 daily doses) or partial (14 daily doses, or less) course of treatment is begun when the animal is proved, or presumed, rabid.

Discuss the clinical manifestations and treatment of arachnidism (black widow spider bite).

The black widow spider (*Lactrodectus mactans*) is the only spider in this country whose bite is poisonous to man. Often the victim is unaware of being bitten, as there is little local pain or reaction. However, within 20 to 60 minutes, rather severe cramping pains of the muscles nearest the bite occur, which spread to the muscles of the back, chest, thighs, and abdomen; boardlike rigidity of the abdominal muscles may simulate acute intra-abdominal disease or tetanus. Feeble pulse, stupor, delirium, or convulsions may follow. The toxin stimulates the myoneural junction or nerve endings directly. For the most part, treatment is directed toward the relief of pain (only an occasional death has been reported). Narcotics and hot tub baths constitute the best forms of therapy. If antivenin is available, it is worthy of trial, as it is generally effective in relieving the severe pain, and no adverse after-effects have been noted. Calcium gluconate 10 per cent solution, 10 ml. intravenously; magnesium sulfate 25 per cent, 25 ml. intravenously; or neostigmine methyl sulfate 1:2000 solution, 2 ml. plus atropine sulfate 0.4 mg. subcutaneously may be given. Likewise, corticotropin (ACTH) is worthy of trial.

CENTRAL NERVOUS SYSTEM AGENTS

What are anesthetic agents?

Anesthetic agents are substances that through their central nervous system depressant action abolish all modalities of sensation and produce a loss of consciousness. In addition to the loss of sensation and consciousness, varying degrees of ablation of motor activity can be produced.

What is the characteristic pattern of activity of anesthetic agents in the central nervous system?

The characteristic feature of anesthetic action is the selective depression of the various levels of the central nervous system. The cortical centers are initially depressed, followed by depression of the spinal centers, and finally the medullary centers. Although there is considerable variation in the speed with which these various centers are depressed, the depth of anesthesia can be divided into four stages, which are indicative of this descending paralysis.

Characterize the stages of anesthesia.

Stage One: Stage of analgesia. Depression of the higher cortical centers.

Stage Two: Delirium or excitement, paralysis of higher motor centers with release of lower motor mechanisms. Consciousness is lost in this stage.

Stage Three: Surgical anesthesia—resulting from the selective depression of the lower spinal centers with muscular relaxation and diminution of spinal reflex activity. Initial depression of medullary function may occur during this stage.

Stage Four: Medullary paralysis resulting from the complete depression of the respiratory center and circulatory collapse. Death results unless there is a rapid reversal of the conditions characteristic of this stage.

What are the objectives of pre-anesthetic medication?

(1) To numb sensation and consciousness for smoother induction of anesthesia.

(2) To prevent respiratory depression.

(3) To diminish secretions of the respiratory tract and the salivary glands.

(4) To prevent cardiac arrhythmias.

(5) To augment the activity of certain anesthetics so as to obtain complete surgical anesthesia without the production of hypoxia, such as occurs with nitrous oxide.

Discuss the advantages and disadvantages of ether, cyclopropane, nitrous oxide, vipental, and procaine intraspinally as anesthetic agents to be used for the maintenance of anesthesia during a long operation in the upper abdomen.

A. Ether: ADVANTAGES: (1) Relatively high potency for good muscular relaxation, (2) thoroughly comfortable safety factor between respiratory and circulatory depression, (3) relatively benign circulatory activity, (4) ease of administration, and (5) relative low cost.

DISADVANTAGES: (1) Irritation of the respiratory tract, which results in excessive bronchial and salivary secretions; (2) circulatory depression in third stage anesthesia due to small muscular relaxation and responsible for the decreased tolerance to hemorrhage and the decreased reactivity to transfusion in this stage of anesthesia; (3) gastrointestinal irritation which produces nausea and vomiting through a central phenomenon and a relative high incidence of postoperative ileus: (4) decreased renal blood flow and kidney irritation; (5) stimulation of the adrenal glands for epinephrine secretion, which produces a hyperglycemia and tachycardia.

B. Cyclopropane: ADVANTAGES: (1) A wide margin of safety between anesthetic and toxic concentrations, (2) relatively rapid induction, (3) nonirritating property as far as the respiratory tract is concerned, (4) rapid recovery, (5) permits the use of relatively high concentrations of oxygen, (6) good relaxation of the musculature.

DISADVANTAGES: (1) Its inflammable and explosive properties, which require special administration techniques with a closed system, (2) laryngospasm by way of overactivity of the parasympathetic nerves, requiring endotracheal tubes to maintain an adequate airway for preliminary ventilation, (3) quiet respiratory activity leading to the retention of carbon dioxide, (4) sensitization of the myocardium producing cardiac arrhythmias, (5) production of postoperative hypotension.

C. Nitrous Oxide: ADVANTAGES: (1) Pleasant for the induction of anesthesia, (2) relatively nonirritating to the respiratory tract.

DISADVANTAGES: (1) Inadequate for the maintenance of stage three surgical anesthesia when used alone, (2) the use of curare or other muscular relaxants is required for complete muscle relaxation for surgery, (3) tendency to produce anoxia when used in concentrations to produce a satisfactory surgical anesthesia, (4) sensitization of the carotid body with the sudden development of respiratory arrest, which may progress to death.

D. Thiopental (Pentothal): ADVANTAGES: (1) Rapid rate of action and pleasant induction, (2) lack of gastrointestinal irritation and vomiting, (3) freedom from salivation and bronchial secretions, (4) generally adequate relaxation, (5) absence of explosive properties, (6) relatively quick elimination in metabolism, (7) low incidence of postoperative complications.

DISADVANTAGES: (1) Respiratory depression, (2) requirement of oxygen therapy for anoxia due to respiratory depression, (3) laryngospasm and bronchial constriction which may occur during anesthesia, (4) requirement of a relatively skilled anesthetist to control the anesthesia.

E. Spinal Procaine Anesthesia: ADVANTAGES: (1) Excellent muscular relaxation, (2) patient remains conscious during the procedure (may or may not be an advantage), (3) relatively little effect on diabetic or renal disease, (4) quite safe in the presence of chronic pulmonary disease because of its lack of respiratory irritation and depression.

DISADVANTAGES: (1) Relatively short action which requires special techniques or other drugs to maintain anesthesia for long periods of time, (2) relative high susceptibility of the respiratory apparatus to the effects by virtue of the effects on the diaphragmatic nerves, (3) reduction in blood pressure and cardiac output because of the resulting arteriolar dilatation from the blocking of sympathetic nerves, (4) occasional appearance of neurological complications, (5) nausea and vomiting as well as hypermotility of the bowel resulting from interference with the autonomic innervation of the gut.

Name four contraindications for general anesthesia.

(1) Advanced age, (2) heart disease with cardiac decompensation, (3) advanced respiratory disease, (4) advanced renal disease.

What are the contraindications to the use of spinal anesthesia?

Disease of the spine, such as severe scoliosis, hypertrophic arthritis, etc., which make lumbar puncture difficult; tuberculosis, metastatic lesions, pathological fracture, and chronic backache. Central nervous system disorders, such as chronic encephalitis, poliomyelitis with residual symptoms (headaches, migraine); lesions of the spinal cord; history of any untoward reaction during or after previous spinal anesthesia. A dermatitis or unfavorable skin condition over the lumbar spine is a contraindication. Severe hypotension, or coronary artery disease, low blood volume, hemorrhagic blood dyscrasias, and extremely unstable, hysterical types of personality are contraindications to spinal anesthesia.

What are the various methods of administering ether?

Ether may be administered by the open or closed method. The administration of ether may be preceded by the inhalation of nitrous oxide, cyclopropane, or other anesthetic agents (mixed anesthesia). Ether may also be administered by rectum. In this method it is mixed with olive oil in the proportion of 3 parts of ether to 1 of oil. For anemic patients the mixture should be 3 of ether to 2 of oil.

What is ethylene?

Ethylene is a colorless gas possessing a sweetish odor and taste and is used as an anesthetic agent by inhalation. The rapid induction of surgical anesthesia can be accomplished with a mixture of 90 per cent ethylene and 10 per cent oxygen. However, it is safer and preferable to use the mixture with at least 20 per cent oxygen and 80 per cent ethylene.

What is basal anesthesia? Give examples.

A form of anesthesia by which the patient is rendered nearly comatose by the presence in the body of a sufficient amount of depressant agent to produce sleep or unconsciousness. Many minor procedures can be carried out with no further anesthesia, but major operations require additional anesthesia. The chief basal anesthetic agents are tribromoethanol (Avertin) and barbiturates.

Discuss general types of local anesthetic agents.

Local anesthetic agents can be roughly divided into two types: those producing anesthesia by physical means, such as extreme chilling, and secondly, those that produce their effect through a chemical action or depressant activity, specifically on the nerve endings or on the nerve fibers. An example of the first group is ethyl chloride, which when sprayed onto the surface of the skin produces a rapid lowering of tissue temperature. The commonly employed local anesthetic agents include in their chemical structure tertiary amino esters of aromatic acids. These substances bring about a reversible depression of the nerve fiber endings when introduced into the surrounding tissues. In contrast to the action of this group are certain other substances, such as quinine, which produce their effects due to surface toxicity and irritation.

Compare the actions of cocaine and procaine as local anesthetic agents.

Cocaine is characterized by relatively high toxicity, relatively slow detoxification by the liver, usefulness limited to topical application for surface anesthesia because of the toxicity, central nervous system stimulation, and the development of addiction and tolerance after systemic use. *Procaine* is approximately one fourth as toxic as cocaine, and it is much more rapidly detoxified by the liver. Its lack of vasoconstrictor activity enhances the absorption of procaine, but this can be overcome by the use of epinephrine in conjunction with procaine as an injectable anesthetic. The degradation products of procaine hydrolysis are relatively nontoxic. The chief disadvantage to the use of procaine is the development of idiosyncrasy or hypersensitivity reactions.

Describe the symptoms of cocaine poisoning.

The first effects of the toxic dose, either by mouth or by subcutaneous injection—unless the case proves rapidly fatal, as sometimes happens—are sensory and mental. The face is hot and flushed, the head feels full, the skin of the body generally is hot so that the subject sometimes disrobes completely. There are exhilaration and great mental activity with restlessness and excitement. Ideas of aggrandizement and self-consciousness occur as in alcoholic intoxication. The pulse becomes rapid and irregular, respirations are increased, the temperature is elevated and there is profuse sweating. Later, the throat becomes dry. The pupils are dilated and react badly to light. Motor symptoms appear, characterized by twitching of the face, staggering gait, and finally clonic and tonic convulsions. The convulsions are usually followed by coma. Sometimes delirium and even maniacal attacks precede death. If the patient recovers there is a protracted convalescence marked by digestive disturbances, headache, muscular weaknesses, and great mental depression. In some cases the fatal termination comes on so rapidly that there is no time for the development of the above symptoms.

Discuss hypnotic and sedative action of central nervous system depressants.

Central nervous system depressants are characterized by their depression of the brain and raising of the threshold for cerebral stimuli. Motor reactivity, autonomic reactions, intellectual activity, and the psyche are all depressed. This depression results in a state which is characterized by lassitude and a loss of emotional tensions and anxieties. Physical activity is markedly decreased. Such an action is called the sedative action of central nervous system depressants.

By comparison, agents that have a more remarkable depressant effect on the central nervous system so as to produce sleep are hypnotics. Hypnosis may be produced by a variety of agents, including those which primarily relieve insomnia that is due to nervousness and allied conditions and those which relieve insomnia due to pain. The barbiturates are an example of the former group; morphine is an example of the latter group.

Name drugs that are commonly used for hypnotic action and give the appropriate dosage.

AGENT	DOSAGE	ROUTE OF ADMINISTRATION
Morphine	8 to 30 mg.	Hypodermic injection
Scopolamine hydrobromide	0.5 mg.	Hypodermic injection
Chloral hydrate	0.5 to 1 gm.	By mouth
Paraldehyde	3 to 8 ml.	By mouth
Phenobarbital	0.1 to 0.2 gm.	By mouth
Sodium phenobarbital	5/100 to 0.2 gm.	By mouth
Pentobarbital	5/100 to 0.2 gm.	By mouth
Secobarbital	0.1 to 0.2 gm.	By mouth

What is propoxyphene (Darvon)?

This is a recent synthetic analgesic used as a substitute for codeine.

What are the general principles of treatment for acute barbiturate poisoning?

In all cases, immediate consideration should be given to the prevention of further absorption of the barbiturates: gastric lavage to remove unabsorbed material, as well as neutralization by solutions of potassium permanganate. Secondly, all cases should receive thoughtful consideration for nursing care during the period of time in which consciousness is lost. These two general measures may be sufficient for the recovery of most cases of mild to moderate intoxication with the barbiturates. Severe cases will require in addition the maintenance of respiratory movements and the prevention of anoxia. The support of blood pressure should be accomplished through the use of fluids and pressure agents. Phenylephrine (Neo-Synephrine) intramuscularly and, if necessary, cortisone intravenously. Only in the most severe cases should the use of analeptic drugs be considered for restoration and maintenance of respiratory reflexes, as well as to lessen other evidences of central depression. Analeptic drugs should be used in doses short of those producing convulsions. Convulsions may increase anoxia and lead to further central nervous system depression. Recently, hemodialysis has proved to be a valuable adjunct in the treatment of acute barbiturate poisoning, for the artificial kidney removes barbiturate from the blood stream 20 times as fast as does the normal kidney.

What are the most important complications of drug addiction?

The concomitant addiction to barbiturates, multiple abscesses at site of injection, homologous serum hepatitis, and metastatic lesions throughout the body as a result of bacteremia from unsterile intravenous injection.

What drugs are most likely to produce addiction?

Morphine, diacetylmorphine (heroin), dihydromorphinone (Dilaudid), methyldihydromorphinone (Metopon), ethylmorphine (Dionine), Pantopon, levorphanol (Levo-Dromoran), codeine, meperidine (Demerol), methadone, alphaprodine (Nisentil), marihuana, and cocaine.

Describe the therapeutic uses of chloral hydrate. Describe the effects of a toxic dose of chloral hydrate.

Chloral hydrate is useful to produce hypnosis in cases of insomnia in which pain is not a conspicuous feature. The sleep produced by normal doses is physiological sleep, but large doses frequently cause hangover. The cardiac depressive actions ascribed to this drug are generally seen only in toxic doses or in cases in which cardiac disease is prominent. The toxic effects of chloral hydrate include severe central nervous system depression with stupor, vasodilatation, low blood pressure, and a rather marked fall in body temperature.

Mention the conditions in which the bromides are useful, and mention principles of dosage.

Bromides are useful for their sedative effect when overexcitement is present, such as occurs in epilepsy, hysteria, alcoholism, convulsions, nervous insomnia, headache, migraine, and neuralgia. They have been used to prevent seminal emissions in cases of hyperesthesia of the sexual organs. The bromides are generally given in large doses (3 to 5 gm./day) until the bromide effect is obtained. This effect is then maintained by smaller doses at infrequent intervals.

Discuss the pharmacologic activity of paraldehyde.

Paraldehyde is a central nervous system depressant which produces a normal sleep. It may be given by mouth but has an unpleasant taste and odor. Its toxicity is relatively low, and it has a wide margin of safety. Detoxification in the body accounts for most of a given dose, and the liver is considered to be most important in this action. Pulmonary and renal excretion account for the remainder.

What are the therapeutic uses of alcohol?

Ethyl alcohol can be used externally as a cooling agent or as a skin disinfectant; it may be used as a solvent for both external and oral medicaments and may be used as a skin wash to remove the irritants in both phenol burns and on exposure to poison ivy. It has been used as a stomachic to increase the appetite. When injected locally, nerve block and ganglionic blockade can be accomplished for relief of pain. Administered by mouth, it is mildly depressant and may be used in the management of insomnia and occasionally in angina pectoris. To achieve a peripheral vasodilatation, large doses are required, which border on intoxication; for this reason, it generally is considered unsatisfactory for this purpose.

What are the general principles in the management of alcoholism?

(*a*) Complete withdrawal of alcohol; (*b*) the induction of quiet sleep with either paraldehyde or chloral hydrate; (*c*) general nursing care until the patient recovers; (*d*) fluids in relatively large quantities, since dehydration is a frequent complication; (*e*) a soft, palatable, high vitamin, high caloric diet; (*f*) the use of chlorpromazine to facilitate withdrawal and control the symptoms thereof; (*g*) the institution of psychotherapeutic measures once the patient recovers; (*h*) the possible employment of tetraethylthiuram disulfide (TETD, Antabuse) to "sensitize" the patient to alcohol.

Discuss the use of tetraethylthiuram disulfide (TETD, Antabuse) in chronic alcoholism.

The ingestion of small amounts of alcohol by patients medicated with TETD produces a variety of undesirable symptoms (TETD = alcohol response) due to the increased concentration of acetaldehyde in the body. When given alone, TETD does not increase the acetaldehyde concentration in the body but when alcohol is given to a TETD-treated patient, the enhanced acetaldehyde level that follows is due to the inhibition of the oxidation of acetaldehyde formed during the intermediate metabolism of alcohol. Thus, if, after a drying-out period of 5 days, a patient suffering from chronic alcoholism is given TETD, which by itself is usually well tolerated for 5 days, and then is given small doses of alcohol (under 50 ml.), the symptoms of the "acetaldehyde syndrome" soon follow. These symptoms include flushing of the body and especially of the face, pulsating headache, tachycardia, irritation of throat, etc. When more than 50 ml. of alcohol is ingested, the above symptoms become more prominent and additional symptoms are observed—nausea, vomiting, blurred vision, vertigo, chest pain, sweating, etc. Once a patient has experienced the ill effects of the "acetaldehyde syndrome" and realizes what a small amount of alcohol will produce them, it follows that alcohol should be eliminated as long as TETD is being administered. Sensitization to alcohol lasts for 6 to 12 days after the ingestion of TETD is stopped. TETD is a potentially dangerous drug and should be used with caution. It is not a cure for alcoholism, but it does afford a period of sobriety during which the patient and physician have an opportunity to obtain a better insight into the various problems connected with the disease.

Discuss the nature of anticonvulsive drugs used in epilepsy.

Anticonvulsive drugs are agents used to prevent epilepsy by suppressing the abnormal focal discharges of brain lesions or by preventing spread to other brain cells without producing severe depression of the central nervous system or other organs. Anticonvulsants should be chosen with consideration for the type of seizure. At present, in grand mal seizure, diphenylhydantoin (Dilantin Sodium) has been used most effectively; it is also effective in psychomotor seizures. Trimethadione (Tridione) and paramethadione (Paradione), methsuximide (Celontin), or phensuximide (Milontin) may be more effective in the individual patient and also may have the advantage of being less likely to precipitate major attacks. Barbiturates and bromides have a general depressant action.

What are the analgesic, antipyretic drugs?

Agents which are capable of decreasing mild pain and lowering body temperature. They are divided into three classes: (1) the salicylates (sodium salicylate, acetylsalicylic acid [aspirin]), (2) para-aminophenol derivatives or "coal tar" antipyretics (acetanilid and acetophenetidin [Phenacetin]), (3) pyrazolone derivatives (aminopyrine, antipyrine [Phenazone], and phenylbutazone [Butazolidin]). Phenylcinchoninic acid (cinchophen) also possesses the combination of weak analgesic and antipyretic action but is considered relatively toxic for these actions, except in gout, where its relief of the acute attack and prophylactic use are firmly established, although the mechanism of action in uric acid metabolism is still undefined.

Discuss the action of acetylsalicylic acid.

After absorption, the drug is rapidly hydrolyzed and circulates as sodium salicylate. Analgesia is accomplished by a selective central depression; it is ineffective against pain of high intensity and is inferior to codeine or the opiates. Defervescence is accomplished by a central action on the hypothalamus and higher cord centers; it is enhanced by sweating, which also occurs. Children may tolerate the drug badly, and an idiosyncrasy among adults is common. In the presence of rheumatism, larger doses are tolerated; its action is so dramatic in the acute rheumatic joint that it is often used as a therapeutic or diagnostic test. The uricosuric action is dependent upon large dosage (5 gm. per day, or greater); it may be enhanced by simultaneous administration of alkali. Excessive medication may produce salicylism with roaring in the ears (tinnitus) and headache, electrolyte derangements with acid-base disturbances of the plasma, gastrointestinal disturbances and hemorrhagic phenomena; occasional lowering of the prothrombin concentration may occur with large dosage.

What are the chief characteristics of acute acetanilid poisoning?

The most important symptom of acetanilid poisoning is cyanosis, which is due to formation of methemoglobin in vivo and is apparently due to metabolic products that are formed in the body. It does not affect the red blood cell. Small amounts of sulfhemoglobin may also be formed, which cannot be reconverted to normal hemoglobin. Excessively large doses produce a hemolytic type of anemia; cardiovascular collapse, hepatotoxic effects, and toxic skin reactions may also be seen. Drug fever has been noted.

What analgesic agents have been noted for the high incidence of agranulocytosis?

Aminopyrine (Pyramidon) and phenylbutazone (Butazolidin) both have been proved to be the cause of fatal cases of agranulocytic angina. The neutrophilic leukocytes may entirely disappear and the entire white count consist chiefly of lymphocytes. Phenylbutazone can also produce aplastic anemia or transitory depression of erythropoiesis.

List the important clinical alkaloids of opium, and the percentage in which they occur in opium.

The clinically important alkaloids of opium are morphine, codeine, and papaverine. Their percentage in opium is 10 per cent morphine, 0.5 per cent codeine, and 1 per cent papaverine. Papaverine belongs to the class of benzylisoquinoline derivatives, while the other two belong to the phenanthrene group.

State the source and dose of apomorphine.

Apomorphine is an alkaloid prepared from morphine by the removal of one molecule of water in the presence of concentrated hydrochloric acid. Other important changes occur in the molecular structure which enhance its activity on the chemoreceptor trigger zone to produce vomiting by central mechanisms. The emetic dose is 5 to 10 mg.

Name the three most commonly used preparations of opium, the percentage of opium contained in each, and the dosage.

PREPARATION	OPIUM	DOSAGE
Camphorated opium tincture U.S.P.	4%	4 ml.
Ipecac and opium powder (Dover's powder)	10%	0.3 to 0.2 gm.
Opium tincture (laudanum)	10%	0.6 to 1.5 ml.

Describe the effects of morphine sulfate on the central nervous system.

Analgesia without blocking motor activity. Relief of visceral pain is dramatic.

Sleep may occur along with sedation. Small doses produce euphoria. Morphine depresses the respiratory vasomotor and cough centers in the medulla. The vomiting center is activated apparently by the stimulation of the chemoreceptor trigger zone and by irritation of the vestibular mechanism. Miosis is produced through a central action.

Discuss the therapeutic problems of morphine administration.

(*1*) *Tolerance:* Failure of the depressant action of morphine during repeated and periodic administration. In order to achieve similarly experienced depressions, larger doses must be used. The mechanism of this phenomenon is at present unknown.

(*2*) *Addiction:* The dependence of certain individuals, especially those with personality defects, on regular administration of morphine or opium derivatives to escape reality or to obtain a mental state of exhilaration or euphoria. The period required for addiction to occur varies from a few days to several weeks. Attempts to withdraw the drug are accompanied by symptoms of irritability, weakness, depression, increased secretory activity of many glands, and gastrointestinal irritability. Temperature control is faulty, with alternate sensations of heat and chilliness. These phenomena are known as the withdrawal syndrome.

(*3*) *Idiosyncrasy:* May be manifested in many ways, including nausea and vomiting, central nervous system stimulation with delirium, insomnia, and occasional disturbances of motor function. These symptoms are more commonly seen in the presence of psychoses and febrile states. Allergic manifestations also include urticaria, dermatitis, and pruritus. The drug is capable, in some cases, of producing profound bronchial constriction in instances of bronchial asthma, with further respiratory embarrassment leading to death, but other cases seemingly do well during status asthmaticus with the depressant action.

What are some contraindications to morphine sulfate therapy?

Because of its respiratory depressant action morphine sulfate is dangerous in the presence of severe cyanosis, anoxia, and respiratory depression resulting from cerebral ischemia, increased intracranial pressure, or injury to the brain. Its use in severe chronic emphysematous changes and cor pulmonale is considered hazardous. Liver disease with borderline hepatic insufficiency may allow more rapid and profound respiratory depression with ordinary doses of morphine. It is contraindicated in acute alcoholism, as well as in delirium tremens. It should never be used to control epilepsy or other convulsive disorders.

What is nalorphine (Nalline) and what is its therapeutic usefulness?

Nalorphine is N-allylnormorphine, a congener of morphine, which has a milder but somewhat similar action to that of morphine, except for lack of the striking analgesic effects. By competitive action, it promptly relieves the respiratory and circulatory depressant action of morphine and, therefore, is extremely useful in the treatment of acute morphine poisoning. It may also be used as a diagnostic aid to precipitate withdrawal symptoms in suspected morphine or other narcotic addicts. Another specific morphine antagonist, levallorphan (Lorfan), is about 5 times more potent than nalorphine.

List the dosage, route, and therapeutic usefulness of morphine, meperidine (Demerol), and methadone.

	MORPHINE	MEPERIDINE	METHADONE
Dosage	5 to 20 mg.	50 to 200 mg.	5 to 15 mg.
Route	Oral, I.V., I.M.	Oral, I.M.	Oral, I.V., I.M.
Uses	Sedation, sleep, relief of pain, decreased motility of the G.I. tract, cough depressant, pre-anesthetic.	Sedation, hypnotic relief of pain, smooth muscle relaxant, pre-anesthetic	Relief of pain, cough depressant, occasionally as pre-anesthetic.

Name the commonly used central nervous system stimulants.

Picrotoxin—a botanical extract, which is chiefly useful as an analeptic in barbiturate poisoning. *Pentylenetetrazol* (Metrazol)—a synthetic, organic tetrazol with stimulant activity on the medullary centers, which is chiefly used as a respiratory stimulant. *Nikethamide* (Coramine)—a pyridine derivative with primary action on the medullary centers with improvement in depressed respiration states, such as in acute morphine toxicity, excess barbiturates, or acute alcoholism. *Amphetamine*—a sympathomimetic amine, which, in addition to pressor effects on the circulation, possesses an analeptic action against central nervous system depressants, psychic stimulation effective against fatigue, and a mild analgesic activity. *Strychnine*—an alkaloid which possesses the ability to stimulate the entire nervous system but chiefly the spinal cord. Medullary centers depressed by barbiturates are stimulated, but less safely and effectively than with other analeptic agents.

What are the "tranquilizer" drugs?

Drugs which are capable of producing changes in mood, decreasing agitation in disturbed individuals, and mild sedation without generalized depression are known as "tranquilizer" or ataractic drugs. They include the phenothiazine group—chlorpromazine (Thorazine), trifluoperazine (Stelazine), prochlorperazine (Compazine), promazine (Sparine), etc.; the propanedial derivatives, meprobamate (Miltown, Equanil), phenaglycodal (Ultran); and the *Rauwolfia* derivatives, such as reserpine (Reserpoid, Serpasil, etc.).

Discuss the untoward reactions of the phenothiazine group of drugs.

In varying degrees, the untoward reactions of this group include Parkinson-like symptoms, agranulocytosis, allergic phenomenon, drowsiness, fever, jaundice ("bile regurgitation" type), miosis, seizures, skin lesions, tachycardia, confusional states, depression, increased appetite, engorgement of breasts, dry mouth, dyskinesia, and vomiting.

AUTONOMIC NERVOUS SYSTEM AGENTS

What are the autonomic drugs?

Agents which act directly on the autonomic effector cells and produce an action similar to the activity of the autonomic nervous system are known as autonomic drugs.

List the effective autonomic agents.

The natural agents associated with stimulation of the sympathetic nervous system are epinephrine (Adrenalin) and levarterenol (*l*-arterenol, *l*-norepinephrine, *l*-noradrenaline). Synthetic or naturally occurring substances that also possess the ability to stimulate sympathetic receptors are ephedrine, phenylephrine (Neo-Synephrine), isoproterenol (Isuprel, Aludrine), amphetamine (Benzedrine), and dextroamphetamine (Dexedrine).

The agents producing stimulation of the parasympathetic receptor cells are naturally occurring acetylcholine and the other choline esters—methacholine (Mecholyl), carbamylcholine (Carbachol), and bethanechol (Urecholine). Similar action can be obtained by inhibitors of cholinesterase, such as physostigmine (Eserine), neostigmine (Prostigmin), and diisopropylfluorophosphate (DFP). Certain alkaloids that occur naturally in plants and seeds, such as pilocarpine and arecoline, are capable of also stimulating exocrine glands and smooth muscles.

What is meant by autonomic blockade? Give examples of such action.

Autonomic blockade is accomplished by either inhibiting the structures stimulated by autonomic fibers or by interfering with transmission in autonomic ganglia. Agents which will inhibit the organs that are innervated by post ganglionic cholinergic nerves include atropine, scopolamine, and other synthetic agents, such as homatropine, methantheline (Banthine), propantheline (Pro-Banthine), diphenmethanil, methyl sulfate (Prantal), pavatrine, adiphenine (Trasentine), and amprotropine (Syntropan). Agents that are effective in blocking the structures stimulated by adrenergic nerves are the beta-haloalkylamines, such as dibenamine and dibenzyline; the ergot alkaloids (ergotamine, ergotoxine), including the dehydrogenated derivatives (Hydergine), the imidazolines (Tolazoline, Priscoline), and phentolamine (Regitine); and benzodioxans (piperoxan [Benodaine]).

Certain substances are capable of blocking neuromuscular transmission or of interrupting ganglionic synaptic transmission; such substances include curare and succinylcholine in the first group, while penta-, hexa- and decamethonium compounds, as well as tetraethyl ammonium (TEA) are examples of ganglionic blockers.

Discuss the nicotinic and muscarinic effects of acetylcholine.

The stimulating effects of acetylcholine and muscarine on smooth muscle and the exocrine glands are quite similar. Acetylcholine also possesses activity in stimulating skeletal muscle and ganglia that is quite comparable to nicotine which, in low doses, stimulates and then, in higher concentrations, paralyzes the same structures.

What are the chief pharmacologic actions of neostigmine (Prostigmin)?

Neostigmine, by blocking the action of cholinesterase, elicits actions similar to those of physostigmine (Eserine). It augments gastric activity and secretion; it increases esophageal tone and peristalsis; it increases the motility of the intestinal tract, especially in the presence of abdominal distention due to atony of the bowel. It produces contractions of small muscle in the urinary tract and does assist in the elimination of urine. Its action on skeletal muscle suggests a direct stimulating effect as well as an intensification of the action of acetylcholine; in these actions, it is particularly useful in the management of myasthenia gravis.

What are the important actions of atropine?

Atropine stimulates local areas of the central nervous system. It is active especially in mild depressions of the medullary centers. It blocks the action of cholinergic drugs on the stomach and intestines to decrease secretory and motor activity. It produces cardiac acceleration by blocking the vagus nerve. It has major activity in the eye by relaxing the sphincter muscle of the iris and the ciliary muscle. It decreases tone and contractions in the bladder muscle and ureter, in the bile ducts, and, to a lesser extent, in the uterus. It may also prevent bronchial constriction by cholinergic stimuli and reduction of bronchial secretions.

What are the differences in action on the heart and circulation of epinephrine and levarterenol?

Epinephrine causes an increased heart rate, augmented cardiac output, peripheral vasodilatation except in cutaneous vessels, decreased peripheral resistance, and an increase in blood flow to the cerebral splanchnic and muscular circulatory beds. Levarterenol (Levophed) generally causes cardiac slowing by way of the vagal reflexes, decreases cardiac output, markedly increases the blood pressure through peripheral vasoconstriction and increases the total peripheral resistance.

What are the chief reasons that some patients in shock do not respond to norepinephrine?

Failure of the smooth muscle of the blood vessels to constrict because of injury by trauma or toxic products; inadequate blood volume; ventricular failure; inadequate dosage (whereas some patients respond to 1 or 2 micrograms per minute, others require larger and more prolonged doses); inadequate distribution of the drug to required vascular areas.

What actions account for the usefulness of ephedrine?

Ephedrine produces a vasoconstriction with rise in blood pressure; stimulation of cardiac action, with increase in heart rate and output; relaxation of bronchial musculature, as well as the smooth muscle of the gastrointestinal tract; and increases in metabolism. It causes active dilatation of the pupils. Its action of decongesting the nasal mucosa permits relief of acute and chronic rhinitis and vasomotor rhinitis.

List the therapeutic applications of adrenergic blocking agents.

Tetraethylammonium (TEA), dibenzyline, and dehydrogenated ergot derivatives (Hydergine) have been utilized in the management of essential hypertension. In the diagnosis of pheochromocytoma, the benzodioxans (Benodaine) and phentolamine (Regitine) are useful. The relief of peripheral vascular spasm has been accomplished by the beta-haloalkylamines (dibenamine, dibenzyline), ergot (Hydergine), and imidazoline drugs (Priscoline).

Discuss the toxicity problems of clinical curare therapy.

Because of its depressant action on neuromuscular transmission, this drug should be limited in use to those physicians trained to manage respiratory depressions. Overdosage results in paralysis of skeletal and diaphragmatic muscles. Maintenance of an airway with adequate ventilation is necessary for recovery. Hypotension may also occur at the height of its action.

What are the pharmacologic actions of antihistamines?

The antihistamines block the action of histamine by preventing reception on the affector cell. They are capable of preventing to a greater or lesser degree the bronchial muscular spasm and other smooth muscle spasms evoked by histamine. They can diminish the cutaneous response of whealing and flair as well as afford some protection in anaphylactoid shock. They may cause central nervous system stimulation but usually depression results. Anesthetic actions have also been described.

Give the treatment for poisoning with antihistaminics.

Severe or fatal poisoning may result from relatively small doses (100 mg.) of the commonly used antihistamine drugs. The symptoms include excitement, hallucinations, ataxia, and convulsions, with fever, flushed face, and fixed dilated pupils. Treatment consists of gastric lavage; ether in oil (50 per cent solution) may be instilled, 0.5 to 1 cc. per kg. of body weight, for cortical irritation; comatose patients are given amphetamine sulfate parenterally as needed.

What are anorexigenic agents?

Anorexigenic agents may be defined as substances that tend to suppress appetite or hunger sensation, or both. Attempts to control appetite may be divided into three categories: (1) substitution of a more pleasurable or more relief-giving stimulus than food ingestion; (2) distraction of attention from appetite to environment; and (3) alteration of appetite perception so that food ingestion is no longer a primary source of pleasure or relief. The first two possibilities are likely to be impractical or socially unacceptable; the third alternative has been receiving the most attention and probably represents the desired action of anorexigenic drugs. Such agents may influence primarily either central or peripheral mechanisms concerned with food intake. However, it is likely that no such drug alone will ever cure obesity. This is, perhaps, fortunate in that excessive appetite reflects a need for pleasurable sensation or relief from psychic discomfort. If a truly effective anorexigenic drug should depress the appetite, it might produce habituation other than excessive food habituation, or neuroses more incapacitating than those of which obesity may be a symptom.

CARDIOVASCULAR DRUGS

What are the cardiotonic drugs?

Those agents which improve cardiac output in the failing heart are sometimes referred to as cardiotonic drugs. The primary group of agents is the cardiac glycosides, while the xanthines and sympathomimetic agents are considered clinically as of value under certain circumstances in which support of the circulation is needed.

What agents comprise the cardiac glycosides?

The purified cardiac glycosides are (*a*) from the digitalis plant: (1) digitoxin, (2) digoxin, (3) gitoxin, (4) gitalin; (*b*) from strophanthus seeds: (1) K-strophanthin-β and (2) ouabain.

What are the actions of cardiac glycosides on the cardiovascular system in failure?

(1) Increased force of myocardial contraction, (2) cardiac slowing, (3) delay in or blocking of A-V conduction, (4) decreased venous pressure.

What are the chief electrocardiographic manifestations of digitalis activity?

(1) Prolonged P-R interval, (2) depression of the RS-T segments, (3) inversion of T waves, (4) shortened Q-T intervals, (5) ectopic beats or premature ventricular contractions, (6) auricular tachycardia, (7) ventricular tachycardia, (8) ventricular fibrillation, and (9) cardiac standstill.

Compare the actions of quinidine and digitalis on the heart.

CHARACTERISTICS	RESPONSES FOR QUINIDINE	RESPONSES FOR DIGITALIS
Action	Depressant	Stimulant
Refractory period	Increased	Decreased
Effects on S-A node	Depressed	Slightly depressed
A-V conduction	Slightly decreased	Major decrease
Strength of myocardial contraction	Decreased	Increased

Discuss digitalis intoxication.

Many of the toxic responses to digitalis are extensions of its therapeutic effects and, for this reason, it is important to make careful observations for possible toxic actions of the drug. When administering digitalis, one should remember that, when given in doses sufficient to be effective, it may also cause poisoning when given in excess. As a rule, anorexia is the first evidence of digitalis overdosage. Conversely, an increase in appetite is usually the earliest evidence of improvement when digitalis is employed in patients with cardiac decompensation. Thus, anorexia represents an important symptom as regards digitalis toxicity. Nausea, vomiting, and occasionally diarrhea will follow. Alterations in cardiac rate and rhythm occur in digitalis poisoning. Extrasystoles represent the most frequent cardiac effect of digitalis overdosage. The cardiac rate may be slowed or increased. Paroxysmal, atrial, and ventricular tachycardia, as well as atrial and ventricular fibrillation may arise from digitalis overdosage. Such neurological effects as headaches, fatigue, malaise, and drowsiness are not uncommon, whereas neuralgic pain, particularly of the lower third of the face, may occur. Mental symptoms include disorientation, confusion, aphasia, and even delirium and hallucinations, especially in elderly arteriosclerotic patients. The treatment of digitalis intoxication consists primarily in stopping the drug. However, attention must also be given to other possible complicating factors, especially fluid and electrolyte balance. Not infrequently, as a result of vomiting and/or diuresis from mercurials, the serum potassium level is low, in which case ordinarily nontoxic amounts of digitalis are sufficient to cause toxic effects.

When is quinidine therapy contraindicated?

(1) During acute infections or toxic processes (especially digitalis intoxication), (2) in a seriously damaged heart (coronary occlusion) or one in advanced failure, (3) when the drug is likely to cause an embolism, (4) when there is a history of idiosyncratic reaction, and, (5) if the return to regular sinus rhythm is highly unlikely.

What are the important manifestations of quinidine toxicity?

Cinchonism, hypersensitivity reactions, ventricular tachycardia or fibrillation, and cardiac standstill are significant findings of quinidine toxicity.

What is the action of procainamide (Pronestyl)?

Procainamide (Pronestyl) closely resembles quinidine in its activity on the human heart with cardiac arrhythmias, but is capable of producing rather profound falls in blood pressure when injected in high dosage over a short period of time. Procainamide may be effective in patients who have failed to respond to quinidine, and vice versa.

From what pharmacologic actions do the nitrites gain therapeutic usefulness?

The nitrites are relaxants of smooth muscle throughout the body. In the cardiovascular system all small vessels participate in the response, especially the postarteriolar vessels. The main effect is a decreased total peripheral resistance with increased blood flow, which is accompanied by a fall in blood pressure. The action is generally of short duration but affords, in cases of angina pectoris, a means of equilibrating cardiac work with the metabolic exchanges of an impaired coronary circulation. Such preparations as amyl nitrite pearls, glyceryl trinitrate tablets (nitroglycerin, Trinitrin), and sodium nitrite are readily absorbed from the lungs, from under the tongue, and from the intestinal tract, respectively, and thus produce an immediate but transient action, whereas erythrityl tetranitrate (Erythrol) and pentaerythritol (Peritrate) are slowly absorbed from the intestinal tract, which largely accounts for their delayed and protracted duration of action.

List the indications for anticoagulant therapy.

The anticoagulants, heparin and bishydroxycoumarin (Dicoumarin, Dicumarol) and the congeneric substitutes (Tromexan, etc.), are designed to prevent intravascular clotting and are indicated in the following conditions: (1) in sudden arterial occlusion from thrombosis or embolism; (2) in primary or postoperative thrombophlebitis and phlebothrombosis, especially of the lower extremities; (3) in vascular surgery; (4) as a prophylactic measure postoperatively in patients with a history of intravascular clotting; and (5) therapeutically and prophylactically in various cardiovascular diseases, such as myocardial infarction, thromboangiitis obliterans, atrial fibrillation with repeated embolic phenomena, etc.

Compare the advantages and disadvantages of heparin and bishydroxycoumarin (Coumarin, Dicumarol).

Heparin and bishydroxycoumarin (Dicumarol, Dicoumarin) and its congeneric substitutes are effective anticoagulants and usually complement each other in their uses. However, certain advantages as well as disadvantages are concerned with each drug. Heparin has a more rapid anticoagulant action but the duration of action is less, which means frequent parenteral administration (1 to 3 hours intravenously, 12 to 24 hours intramuscularly or subcutaneously), which are both troublesome and costly. Dicumarol is effective with daily oral dosage and is relatively inexpensive. However, the laboratory control of heparin therapy offers an advantage over that of Dicumarol in that determination of coagulation time is usually more accurate and less expensive than the determination of prothrombin activity. Both drugs possess potential toxic effects. The chief danger from heparin is hemorrhage (hematomas, hematuria, etc.), and an occasional patient hypersensitive to heparin may experience a sensitivity reaction to it. With Dicumarol, hemorrhages may also occur, but the margin of safety seems more satisfactory.

Discuss the "lipemia clearing" action of heparin.

Plasma lipids, including cholesterol and phospholipids, combine with plasma protein to form lipoproteins, complexes of which have been shown by the ultracentrifugal flotation technique to have varying particle weight. During periods of fat absorption there is a transient elevation of molecular classes of higher density, often with the development of turbidity of the plasma. This turbidity is dispelled by administration of heparin, which apparently reacts with some tissue factor (heart, lung) to produce a "clearing factor" that causes a shift in the lipid distribution pattern toward molecules of the lower density classes. This "lipemia clearing" action of heparin is apparently not fundamentally related to its anticoagulant effect. The possible importance of heparin in the regulation of the plasma lipoprotein pattern is indicated by reports that it protects against the development of atherosclerosis in cholesterol-fed rabbits and relieves anginal pain in patients with coronary artery disease.

List the contraindications for heparin therapy.

Heparin is contraindicated in the presence of hemorrhagic blood dyscrasias, ascorbic acid deficiency, increased capillary fragility, subacute bacterial endocarditis, suppurative thrombophlebitis, recent surgical procedures on the brain or spinal cord, recent intracranial hemorrhage, continuous tube drainage of the stomach or small intestines, ulcerative or granulomatous lesions, and extensive denudation of skin.

Discuss the diuretic action of acetazolamide (Diamox).

Acetazolamide (Diamox), a diuretic agent, produces its action by depressing tubular reabsorptive transport of electrolytes. In contrast to the mercurial diuretics, it promotes the excretion of bicarbonate ion rather than chloride ion, as a result of its inhibitory effect upon carbonic anhydrase in the renal tubule. Although the diuretic action of acetazolamide is not so rapid or so dramatic as that of the mercurial diuretics, it can cause a steady decline in weight to an edema-free level and is well tolerated orally. Since acetazolamide disturbs the acid-base balance (metabolic acidosis) in a manner different from that of the mercurial diuretics (metabolic alkalosis), it would seem practical, in the rapid mobilization of fluid, to combine their use, each drug being given on alternate days. In this way, one drug would compensate for the disturbance in acid-base balance produced by the other, thereby avoiding refractoriness to either drug.

What are the thiazide derivatives?

Structurally, the thiazide derivatives, chlorothiazide (Diuril), hydrochlorothiazide (Hydrodiuril, Esidrex, Uretic), flumethiazide (Ademol), and hydroflumethiazide (Saluron), as heterocyclic sulfonamides, would seem to be potential carbonic anhydrase inhibitors but they depart sufficiently widely in actions and effects from that group to justify a separate classification. It appears that the primary predominant effect of these compounds is to increase sodium excretion with a lesser effect on chloride excretion. There is actually some carbonic anhydrase inhibitory action in these drugs but it is relatively slight and thus there is very little bicarbonate loss in typical chlorothiazide-type diuresis. From clinical reports it appears that these agents are the most satisfactory diuretics now available.

List the indications and untoward effects of cation exchange resins.

In general, the cation exchange resins are used in conditions in which the restriction of salt is of value (hypertension, congestive heart failure, nephrosis, cirrhosis of the liver, etc.). Since the exchange resins interfere with the intestinal absorption of salt, it is possible to allow a more liberal intake of salt, which simplifies the problems of a low salt diet. In the mobilization of excessive amounts of extracellular fluid, the exchange resins are usually used initially in combination with a mercurial diuretic and, once an edema-free state is obtained, it may be maintained with the exchange resins alone or it may be possible to reduce the frequency with which the diuretic agents are administered. Furthermore, because of the affinity of exchange resins for potassium cations, their administration is often effective in the treatment of hyperkalemia.

Define xanthines.

Caffeine, theophylline, and theobromine are methylated xanthines and are similar in pharmacological action but differ markedly in the intensity of their actions on various structures, particularly on the central nervous system, kidney, myocardium, and smooth muscle. Treatment with the xanthines is accompanied by certain undesired side actions; when given orally they have an irritant effect on the gastric mucosa which limits their usefulness. Likewise, when employed parenterally, they must be given with caution (especially theophylline [aminophylline] intravenously). *Caffeine* (caffeine and sodium benzoate) is a powerful central nervous system stimulant, affecting the entire system, with its main action on the psychic and sensory functions. In addition, especially when administered parenterally, caffeine acts on the respiratory, vasomotor, and vagal centers in the medulla. *Theophylline* (aminophylline) finds its chief usefulness as a bronchodilator drug in the prevention and treatment of asthma; in the relief of paroxysmal dyspnea by increasing cardiac output, decreasing venous pressure, and relaxing bronchial musculature; in the relief of pain in angina pectoris by dilating the coronary vessels; and as a diuretic agent by virtue of its hemodynamic actions, which result in an increased cardiac output, renal blood flow, and glomerular filtration, plus its ability to depress the renal tubular reabsorptive transport of electrolyte. The best results with theophylline as a diuretic are obtained with intravenous administration of the drug, preferably in combination with mercurial therapy. *Theobromine* (theobromine and sodium acetate) possesses the same actions as theophylline but to a lesser degree. When used as a diuretic, the effect is more prolonged.

What are the pharmacologic actions of reserpine (Serpasil, Reserpoid)?

Reserpine, a purified alkaloid isolated from *Rauwolfia,* exerts its action most prominently upon: (1) the cardiovascular system—reduction in arterial blood pressure and slowing of the heart rate, which result from central depression of the vasomotor system; (2) the central nervous system—causes relaxation, tranquilization, and sedation, which do not appear to be due to a generalized central depression but rather to a reduction in attention and responsiveness to external stimuli. No doubt many of the untoward effects of reserpine (miosis, lacrimation, increased intestinal peristalsis, etc.) also result from its actions on the central nervous system.

In what conditions are the veratrum alkaloids employed?

For the most part, the veratrum alkaloids have been used in the treatment of conditions associated with elevated blood pressure, such as essential and malignant hypertension, toxemias of pregnancy, certain renal disorders, etc. Veratrum alkaloids possess desirable vasodepressor properties, such as a widespread reflex vasodilation, which includes the cerebral and renal arterioles; they do not interefere with normal vasomotor lability or reflexes, since they do not paralyze ganglia or adrenergically innervated musculature. In addition, they do not cause postural hypotension, as they do not diminish cardiac output, cause tachycardia, or induce venous pooling. Despite these properties, the veratrum alkaloids have proved disappointing in the treatment of hypertensive states, in that the margin of safety is quite narrow and, because of the high incidence of toxicity, particularly nausea and vomiting, the drug by necessity must be discontinued. However, encouraging results have been obtained with veratrum preparations in reduced dosages, used in combination with other agents and measures, including restricted dietary sodium, hexamethonium, dehydrogenated ergot alkaloids, dibenzyline, hydrazinophthalazine, and *Rauwolfia* alkaloids.

List the contraindications for the use of ergotamine.

Ergotamine should not be used in the presence of infection; in patients with vascular disease, such as thrombophlebitis, advanced arteriosclerosis, Raynaud's or Buerger's disease, etc.; pregnancy; renal or hepatic diseases.

Discuss the mechanism of action and clinical uses of mercurial compounds.

Although the different mercury-containing compounds vary as to their therapeutic effect, depending on their chemical composition, their fundamental action is similar. The mercurials exert their action by interfering with cellular metabolism and function in that the mercuric ion reacts with the sulfhydryl groups to form mercaptides that inactivate these essential enzymes. This action of the mercurials applies to tissue cells as well as to bacteria. As germicidal agents, certain organic mercurials, such as merbromin (Mercurochrome) and nitromersol (Metaphen), applied locally to infected areas exhibit an antibacterial effect without local tissue damage, since the sulfhydryl receptors of microorganisms appear to be more sensitive than those of the host. If mercurous chloride (calomel), a very insoluble salt, is taken orally, it passes through the stomach unchanged and, in the intestines, a portion of the mercurous ions is converted to the more soluble mercuric ion, which produces its action on the epithelial cells of the enteric tract. Thus, the transport mechanism of those cells is interfered with by the mercuric ion, with resulting electrolyte and consequently water retention in the bowel, which phenomenon probably accounts for the cathartic action of calomel. Likewise, the organic mercurials, such as mercaptomerin sodium (Thiomerin sodium), meralluride (Mercuhydrin), chlormerodrin (Neohydrin), etc., which are largely and rapidly excreted by the kidney, exert a selective inhibitory action on the sulfhydryl enzyme systems of the renal tubular cells that are essential for tubular transport energy, thus interfering with the active reabsorptive transport of certain ions. Since the organic mercurials are so completely and rapidly excreted by the kidney and their low dissociability permits control of the degree to which renal reabsorptive capacity is reduced, it is possible to produce functional renal changes with a minimum of local or systemic poisoning by the mercuric ion. Although the mercurials have long been regarded as effective germicides, more recent studies have indicated that the therapeutic index of the various mercurial compounds is low and they fall far short of being ideal germicides. As indicated, mercury bichloride is too irritating and toxic to be applied to the abraded skin surface and its use as an effective insecticide has been replaced by safer and more efficient agents (chlorophenothane [DDT] and benzene hexachloride). Likewise, since the mercurial compounds are relatively ineffective in killing spores, their use in the sterilization of certain surgical instruments which are harmed by boiling is of doubtful value. Finally, the action of mebromin (Mercurochrome) is only bacteriostatic and that of nitromersol (Metaphen), which is greater, does not give bactericidal effects in the concentration commonly employed. However, with high concentrations of mercuric ions obtainable with mercury bichloride (mercuric chloride solution) tissue damage ensues as a result of denaturation and precipitation of the protein molecule. On the other hand, when the insoluble mercury compounds are incorporated in ointment bases, the mercuric ion in low concentrations produces a prolonged action without appreciable tissue damage and is thus employed as an antiseptic agent (yellow mercuric oxide ointment, ammoniated mercury ointment, etc.).

DIGESTANTS

Define digestants.

Digestants are drugs that promote the process of digestion and are employed chiefly as replacement therapy in deficiency states. The most commonly used digestants are: hydrochloric acid and pepsin for the treatment of achlorhydria, pancreatic enzyme preparations (pancreatin) in conditions with deficient secretion of pancreatic juice, such as pancreatitis, and various bile preparations (dehydrocholic acid [Decholin]), ox bile (Bilein), etc., which are employed in cases of organic or functional hepatic insufficiency by virtue of their cholerectic action and effects on intestinal absorption, especially of fats, fat-soluble vitamins, and the activation of pancreatic lipase.

Classify gastric antacids.

(*1*) *Systemic Antacids:* Drugs that are soluble, readily absorbed, and capable of changing the pH of the extracellular fluid and producing alkalosis. For example, sodium bicarbonate in excess of the amount necessary to neutralize the hydrochloric acid of the stomach contents passes into the intestines and, as unneutralized bicarbonate, is absorbed causing an increase in the bicarbonate concentration in the blood and a rise in pH. In order to restore the normal chemistry of the body fluids, the kidney must excrete the excess bicarbonate and thus the urine becomes alkaline. Failure on the part of the kidney properly to eliminate bicarbonate results in alkalosis.

(*2*) *Nonsystemic Antacids:* Substances which form compounds that are not absorbed and thus are less likely to produce alkalosis. For example, magnesium oxide is practically insoluble, the excessive portions remaining in the stomach to react with hydrochloric acid subsequently secreted. Although magnesium oxide neutralizes the gastric acid more slowly than sodium bicarbonate, its duration of action is longer. Magnesium trisilicate, a nonsystemic antacid, also acts as an effective adsorbent by virtue of the formation (in the stomach) of hydrated silicon dioxide, the gelatinous consistency of which provides an adherent coating for the crater of an ulcer, thereby localizing its prolonged antacid effect at the desired site. The hydrated silicon dioxide that forms in the stomach passes into the intestinal tract, where it functions as an effective adsorbent. Aluminum hydroxide, also a nonsystemic antacid, exerts its action by a chemical reaction with hydrochloric acid to form aluminum chloride which, in the intestinal tract, reacts with the alkaline secretions to form basic aluminum salts that are not absorbed. In addition, aluminum compounds inhibit peptic activity by inhibiting the action of the enzyme.

What untoward effects may accompany the neutralization of gastric contents?

The gastric phase of digestion may be retarded by the inactivation of pepsin in the neutral or alkaline media. In addition, the rate of secretion of hydrochloric acid is greater after the administration of an alkali than if it had not been given ("acid rebound").

CATHARTICS

Discuss the actions of cathartics.

Cathartics are drugs that are employed to promote defecation and exert their effect as a result of both their chemical nature and mechanism of action.

(*1*) *The So-called "Irritant Cathartics":* (*a*) The emodin group (cascara sagrada, senna, rhubarb, aloe) exert an irritating action, by virtue of their characteristic active principles, on the large intestine that increases its propulsive movements, causing a rapid passage of fecal contents; (*b*) irritant oil cathartics, such as castor oil, which is hydrolyzed by the fat-splitting enzymes in the intestines to glycerol and ricinoleic acid; the latter, a marked irritant, stimulates the motor activity of the small intestine, causing a rapid propulsion of the contents of the small intestine. (*c*) In addition, there are others, such as phenolphthalein, mercurous chloride (calomel), etc., which, because of their toxic properties, have declined in popularity.

(*2*) *Bulk Cathartics:* (*a*) Saline group —magnesium sulfate (Epsom salt), magnesium citrate (magnesium citrate solution), sodium sulfate (Glauber's salt), sodium phosphate (effervescent sodium phosphate), and potassium sodium tartrate (Seidlitz powders or compound effervescent powders). The saline cathartics cause an increase in the volume of water in the intestines, as a result of water being extracted from the circulation in order to maintain osmotic equilibrium. This increased water volume exerts a mechanical stimulus that increases intestinal motor activity and the fluid is rapidly propulsed and expelled. (*b*) Colloidal, fiber, and emollient group: agar (agar-agar), bran, tragacanth (gum tragacanth), psyllium seed (psyllium hydrophilic mucilloid with dextrose [Metamucil]), and liquid petrolatum (white mineral oil). These cathartics act by increasing the bulk of the intestinal tract and/or as emollients or lubricants that facilitate the passage of feces.

ANTI-INFECTIVE AGENTS

Give the major clinical developments concerned with sulfonamide therapy.

(1) The introduction of poorly absorbed compounds (succinylsulfathiazole [Sulfasuxidine], phthalylsulfathiazole [Sulfathalidine]) that remain in the intestinal tract and produce local changes in the bacterial flora, with little or no systemic toxicity. These are useful in combating infections of the intestinal tract and as prophylactic agents in contemplation of bowel surgery. (2) The use of sulfonamide mixtures as a method of decreasing the incidence and severity of renal toxicity. Chemical and clinical studies have demonstrated that the total amount of sulfonamide that can be held in solution in urine is substantially increased when two or more of these substances are administered simultaneously and that this is accomplished without sacrificing therapeutic activity. Furthermore, such a mixture is more soluble at pH 5.5 and below than any single solu-

ble sulfonamide, such as sulfisoxazole; hence, the rationale for the combination of two or more sulfonamides as a method of decreasing renal toxicity while maintaining antibacterial efficacy in the treatment of susceptible system infections. For such mixtures, sulfadiazine is the common denominator and is usually combined with sulfamerazine for a dual mixture, plus sulfamethazine for a triple mixture. (3) The development of sulfonamides possessing relatively high solubility in urine and hence lowered renal toxicity: sulfisoxazole (Gantrisin), sulfisomidine (Elkosin), sulfamethylthiadiazole (Thiosulfil), which are used successfully in the treatment of urinary-tract infections. (4) More recently, the single-dose, long-acting varieties, such as sulfamethoxypyridazine (Kynex, Medicil) and sulfadimethoxine (Madribon), which are used primarily as prophylactic agents. (5) The establishment of the value of therapy with the sulfonamides in combination with the antibiotics: sulfadiazine plus penicillin in various coccal meningitides, sulfadiazine plus streptomycin in brucellosis, sulfadiazine plus a tetracycline in *H. influenzae* meningitis, etc.

List the shortcomings of sulfonamide therapy.

(1) Many strains of bacteria are naturally resistant to their action. (2) Initially susceptible strains in a species can and do develop resistance to these drugs during treatment, so that a number of bacterial infections are no longer amenable to sulfonamide therapy. (3) These drugs may produce a variety of serious untoward reactions. (4) The antibacterial activity of the sulfonamides is diminished in the presence of pus.

Discuss sulfonamide toxicity.

In general, the incidence and severity of the untoward reactions that follow sulfonamide therapy tend to be influenced by the duration of treatment and total dosage of drugs. Children seem to tolerate these drugs better than the aged; patients with good nutrition and normal renal function, better than the poorly nourished and those having kidney damage. For the most part, the incidence of the more severe toxic reactions is lower with the sulfapyrimidines (sulfadiazine, sulfamerazine, sulfamethazine) than with other sulfonamides that approach their therapeutic effectiveness for systemic diseases. Mild toxic reactions include nausea, vomiting, dizziness, and cyanosis, whereas the more serious are renal complications (hematuria, oliguria, anuria, azotemia), skin lesions, fever, blood dyscrasias (neutropenia, agranulocytosis, anemia of the hemolytic type), hepatitis, nephritis, myocarditis, purpura, and neuritis. In addition to these immediate toxic reactions, these drugs may give rise to changes in the blood vessels simulating periarteritis nodosa.

Describe the mechanisms involved in the development of sulfonamide renal toxicity. Give precautionary measures.

The renal complications represent the most frequent and most dangerous untoward reactions that follow the administration of the sulfapyrimidines (sulfadiazine, sulfamerazine, and sulfamethazine), whereas this hazard is rarely encountered with the use of the more soluble compounds (sulfisoxazole [Gantrisin], etc.). Two main causes have been established for the development of renal complications: (*a*) The nephrotoxic or nonobstructive type, the nature of which is not fully understood, apparently has no relation to the amount of drug in the circulating blood or its concentration in the urine. Fortunately, this type is rarely encountered. (*b*) The mechanical, or obstructive type, which accounts for most of these complications from the sulfapyrimidines, is primarily caused by the intratubular deposition of poorly soluble crystals of the drug, especially the acetyl derivatives. With minor exceptions, crystalluria is found only in acid urine, which is almost always present in patients receiving these drugs without adjuvant alkali therapy. This is partially the result of restricted food intake during the febrile illness, which gives rise to a net balance of acid to be excreted by the kidneys. The solubility of the sulfapyrimidines and their acetyl derivatives in urine increases a great deal with the increasing pH within the physiological range of urinary pH.

In view of these potential renal complications that follow the use of the sulfapyrimidines, it is important to observe certain precautionary measures which may prevent the occurrence, or at least reduce the incidence, of these complications. Certainly a history of previous sulfonamide medication followed by toxicity is in itself a contraindication to further sulfonamide therapy. In addition, in order to augment the excretion of the drug and to avoid undue concentrations in the urine, as well as to lessen the acidity, it is important to maintain the daily volume of urine in adults who receive these drugs at a minimum of 1,500 cc. Since the hazard of precipitation in the urinary tract is decreased by using mixtures of partial dosage of two or three sulfapyrimidines, it is advisable to give such mixtures in the treatment of systemic infections. Furthermore, it is generally agreed that alkaline adjuvants should be used in conjunction with sulfonamide mixtures, especially when large doses of the drug are given. Although the sulfapyrimidines, singly or in combination, represent the sulfonamide of choice in the treatment of susceptible systemic diseases, in those cases in which it seems unwise to use them one may administer the more soluble sulfonamides, especially sulfisoxazole, with a wider margin of safety.

List the indications and contraindications for sulfonamide therapy.

At this time the sulfonamides are indicated in the treatment of uncomplicated urinary-tract infections, bacillary dysentery, meningococcal infections, chancroid, and trachoma, and are used in combination with the antibiotics in certain other types of infections, such as pneumonia, meningitis, and actinomycosis. Furthermore, such drugs as phthalylsulfathiazole and succinylsulfathiazole, which are poorly absorbed and are largely excreted in the feces, are used prophylactically in the preparation for large-bowel surgery. In outbreaks of meningococcal infection or bacillary dysentery, and in prevention of acute hemolytic streptococcal respiratory infections (especially tonsillitis), sulfadiazine is employed.

The only possible contraindication to sulfonamide treatment is a history of a previous sensitivity to sulfanilamide and its derivatives, as manifested by drug fever, gross hematuria, dermatitis, hemolytic anemia, neutropenia, or jaundice. Certainly in patients with such a history one should select some other form of therapy, such as the antibiotics, rather than run the risk of continuing sulfonamide toxicity. In ambulatory patients receiving the sulfonamides, it is best to advise against the use of alcohol, as at times they tend to cause marked dizziness. Aside from this, there seems to be no evidence that any other form of medication or food is contraindicated.

Give the methods of administration and dosage in sulfonamide therapy.

The sulfonamide compounds are administered locally, orally, and parenterally. The local use of these drugs has been practically abandoned because of the relatively high incidence of untoward reactions from this route of administration. In general, their administration by mouth constitutes the most satisfactory method. However, in certain instances, when a rapid elevation of the drug concentration in the blood is desired, or when oral medication is impractical or impossible, it is necessary to resort to parenteral administration. For intravenous therapy with the sulfapyrimidines (sulfadiazine, sulfamerazine and sulfamethazine), a 5 per cent solution of the sodium salt in sterile distilled water is preferred. Parenteral preparations are likewise available for certain of the more soluble compounds.

Several factors influence the amount of drug required to produce the desired result. As a rule, the dosages are smaller when the compounds are used prophylactically than when they are used therapeutically. Patients treated in bed usually are given larger amounts than those who are ambulatory. The type of infecting organism must be considered for its susceptibility to the drug and also whether the infection is mild or severe. Acute conditions, involving soft tissues, require different dosages than do chronic bone or urinary-tract infections. Moreover, certain factors, such as kidney function, drug absorption, and the state of dehydration, all tend to influence the amount of drug found in the blood. From this it becomes apparent that it is impossible to outline a course of sulfonamide therapy that will suit the needs of every patient. Therefore the following recommendations on dosage are for the treatment of adult patients suffering with acute infections severe enough to warrant full sulfonamide dosage. For infants and children the dose schedule is proportioned according to weight and age.

For the sulfapyrimidines (sulfadiazine, sulfamerazine, sulfamethazine) a blood concentration of free drug of 5 to 8 mg. per 100 ml. should give maximum results in most types of infections caused by susceptible organisms. In meningitis, higher concentrations, about 15 mg. per 100 ml., are desirable. Sulfadiazine is preferred in this instance, in that somewhat higher cerebrospinal fluid levels are attained. The desired blood levels can usually be attained by an initial oral dose of 3 to 4 gm. followed by 1 gm. every 4 to 6 hours.

Likewise, the same dose schedule is observed with the various sulfonamide mixtures, the accepted ratios of the sulfonamide combinations being 1:1:1 for triple and 1:1 for dual mixtures. For intravenous use with the sodium salt, the dosage is calculated on the basis of 0.006 gm. per kg. of body weight and is repeated at 6-hour intervals. For the most part the dose schedule for the more soluble sulfonamides is somewhat larger than for the sulfapyrimidines, in that the blood levels are more sustained with the former. However, urine concentrations of the latter group are much greater; hence their usefulness in the treatment of urinary-tract infections. For the relatively nonabsorbable sulfonamides (phthalylsulfathiazole and succinylsulfathiazole), the usual dose is 2 gm. every 4 to 6 hours orally. For the single-dose, long-acting derivatives (sulfamethoxypyridazine [Kynex, Medicil] and sulfadimethoxine [Madribon]), the usual dose is 0.5 gm. daily.

Give the mode of action and therapeutic limitations of penicillin.

Although the exact mechanism of the action of penicillin is not yet clearly defined, it appears that its maximum action is manifested chiefly against rapidly multiplying organisms by interfering with their ability to synthesize protein from amino acids, the process being blocked at a point which allows the accumulation of peptides. Against susceptible microorganisms, its activity may be bactericidal or bacteriostatic, depending upon the concentration at the site of infection. Certain species of bacteria, particularly *E. coli,* are capable of producing an enzyme, penicillinase, which inactivates the drug. The organisms most susceptible to penicillin activity are those in the gram-positive group: pneumococci, streptococci, staphylococci, certain of the clostridia, and strains of lactobacilli. In addition, the gram-negative cocci, meningococci and gonococci are likewise sensitive to this drug. Treponemal and borrelial infections, including syphilis, pinta, yaws, and Vincent's angina, can be successfully treated with this drug. Penicillin in combination with other antimicrobial agents is likewise a valuable adjunct in the therapy of other diseases.

Give an evaluation of oral penicillin.

A preference for the oral over the parenteral route of administration for any medication is freely acknowledged when the two routes have equal therapeutic effect. From the beginning, it was shown that orally administered penicillin was therapeutically effective, but, because acid destroys penicillin, only a fraction of the administered dose was absorbed from the gastrointestinal tract. The exact amount of penicillin G destroyed by acid is not known, but evidence indicates that it is seldom great; phenoxymethyl penicillin (penicillin V) and phenoxyethyl penicillin (phenethicillin) seem actually not to be destroyed at all. The proportion of the ingested dose of penicillin eventually inactivated in the colon, or excreted in the stool, can only be inferred, but the maximum absorption that has been observed under any condition is only about one third of the ingested dose of penicillin G and probably more in the case of the other two compounds. Therapeutically, all three preparations are effective in reasonable doses—200,000 units given 3 to 4 times a day for most of the common penicillin-treated infections. In addition, the more serious allergic reactions to penicillin occur less often after oral administration of the antibiotic.

What are "synthetic" penicillins?

With the preparation and isolation from penicillin fermentations of pure 6-aminopenicillanic acid, several so-called "synthetic" penicillins have been introduced for clinical trial. The first penicillin prepared by chemical synthesis was phenoxyethyl penicillin (phenethicillin), which was first introduced under the name Syncillin in this country and is now marketed under several other trade names (Maxipen, Alpen, Dramacillin S, and Darcil). Originally, phenethicillin was thought to possess certain advantages over other oral penicillins but it would seem from subsequent observations that the major claims (higher blood levels and lower toxicity) for the superiority of phenethicillin over penicillin G or penicillin V are not well founded.

More recently, another "synthetic" penicillin, methicillin (Celbenin and Staphcillin) has become available. The most important property of the antibiotic is the fact that it is minimally, if at all, degraded by staphylococcal penicillinase. Though chiefly valued for its activity against penicillinase-producing staphylococci, the new penicillin is active but to a lesser degree than penicillin G against Group A hemolytic streptococci, *Streptococcus viridans,* and the pneumococcus. Preliminary clinical results with this new antibiotic in the treatment of penicillin-resistant staphylococcal infections are encouraging. However, these studies indicate that allergic manifestations are associated with its use. Since the drug is destroyed by acid in the stomach, it is not effective when given orally. It is rapidly absorbed and excreted after intramuscular injection and is excreted more rapidly after intravenous injection, so that, even after large doses, useful blood levels cannot be found in serum four hours after the former and three hours after the latter. Thus, relatively large dosage (1.0 to 1.5 gm.) is necessary every 4 to 6 hours (approximately 10 million units daily).

Preliminary data on still another "synthetic" penicillin, sodium oxacillin (Prostaphlin), show that, unlike methicillin, it is well absorbed when taken orally and possesses appreciably greater activity than methicillin against nearly all susceptible organisms (including penicillin G resistant staphylococci).

Discuss allergic reactions to penicillin.

Hypersensitivity to penicillin has been observed during recent years in increasing frequency. There are four main types of allergic response to the antibiotic:

(*1*) *Anaphylactic, or Anaphylactoid:* This is the immediate type of reaction in which the patient suddenly develops serious manifestations with collapse and difficulty in breathing and has all the signs of a typical asthmatic with urticaria, etc. From the reported cases, the incidence of fatality is about 10 per cent.

(2) *Serum-Sickness–like Reaction:* The delayed type of serum-sickness–like reaction occurs anywhere from 7 to 10 days after the patient receives penicillin. This is evidenced by fever, urticaria, joint pains, etc.

(3) *Contact Dermatitis:* This is due to contact with the material, either in the form of ointments, powders (as used by nurses or in manufacture), eye drops, aerosols, etc.

(4) *ID Reaction:* In this condition there is a flare-up of infections caused by related fungi, such as an activation of trichophytosis.

Outline measures for the prevention and treatment of penicillin sensitivity reactions.

(1) *Careful History:* Most of the severe reactions have occurred in patients having a history of allergic symptoms from previous administration of penicillin or in individuals usually suffering from asthma, hay fever, or eczema. Hence, the incidence of hypersensitivity reactions to penicillin may be reduced if an allergic history is obtained before administering the antibiotic. However, a careful history will not reveal all the potential allergic reactions, in that prior exposure to unknown sensitization from penicillin-containing milk and its products, foods containing penicillium-type molds (such as Roquefort cheese), the injection of vaccines containing penicillin (poliomyelitis, etc.), the use of penicillin-contaminated syringes, or by the absorption of dermatophytes through the skin may pave the way for a later unpredictable reaction to the therapeutic use of penicillin.

(2) *Diagnostic Tests:* Attempts to predict which patients will react unfavorably to penicillin by means of skin and conjunctival tests are for the most part variable, unpredictable, and not without danger, in that they may give rise to general hypersensitivity reactions. Recently, it has been shown that immunological evidence of penicillin hypersensitivity can frequently be found in patients experiencing penicillin reactions. The hemagglutination technique appears to have a high degree of specificity for the penicillin molecule and may prove to be a valuable tool in the identification of penicillin allergy.

(3) *Oral Penicillin:* Although these reactions may follow any route of administration of penicillin, it is well established that serious allergy to the drug is most likely to occur after parenteral administration, especially after repeated intramuscular injections; whereas the oral route is least likely to initiate severe hypersensitivity reactions. If parenteral penicillin is *absolutely* necessary, the injection should be in the muscles of the upper arm. The substitution of a hypoallergic type of penicillin in a patient giving a history of any sort of reaction to the antibiotic is hazardous. Likewise, antihistamines given concurrently with penicillin may mask valuable warning signals, with anaphylaxis impending when the antihistamine effect wears off.

(4) *Treatment:* In patients suffering from immediate anaphylactic reactions to penicillin, the prompt administration of epinephrine, aminophylline, cortisone, or a derivative, etc., has proved highly effective in many instances. However, many deaths occur before these agents can be administered. The use of antihistamines and penicillinase (Neutrapen) in such cases is of no value, although they may prove helpful in the delayed type of reactions.

Discuss the methods of administration of penicillin.

The plasma or serum concentration of penicillin may serve as a rough guide to the amount of drug in the tissues, the more important consideration being the amount of penicillin occurring at the focus of infection. The amount of penicillin reaching the site of the infection is largely dependent upon three factors. (1) The *rate of absorption* into the blood stream. When administered intramuscularly, penicillin G is rapidly absorbed, whereas repository (depot) penicillin preparations (procaine penicillin G, benzathine penicillin G [Bicillin, Permapen]) provide a tissue depot from which the drug is more slowly absorbed. Absorption from the gastrointestinal tract is relatively slow but sufficient in most types of infections (see Oral Penicillin). (2) The *diffusion rate* into tissues. For the most part, penicillin permeates most tissues, except the brain, cornea, and lens. Also, in relatively avascular areas, such as thick-walled abscesses, the amount of penicillin in the tissues is limited. (3) The *rate of excretion*. Penicillin is rapidly excreted by the renal tubules, thereby making it difficult to maintain a high concentration of the drug in the circulating blood. In order to prevent this rapid urinary excretion of penicillin, various so-called renal blocking agents have been employed, the most useful being probenecid (Benemid).

Although a concentration of 0.03 unit per cc. of plasma or serum is considered a minimum effective therapeutic level and is effective in many types of infection, one may enjoy a false sense of security in relying on this concentration for the treatment of every type of infection susceptible to penicillin. Since the effectiveness of plasma concentrations of penicillin after any dose is dependent largely upon the specific susceptibility of the organism being attacked, it is only in the treatment of more resistant infections that the significance of penicillin plasma concentrations can be clearly interpreted in terms of its relationship to therapeutic effect. In fact, most infections are so susceptible to penicillin therapy that quite frequently little attention need be paid to penicillin plasma concentrations because any of the usual dosage schedules will effectively control the infection.

Discuss the role of streptomycin and dihydrostreptomycin in antimicrobial therapy.

Streptomycin remains uniquely valuable for the treatment of tuberculosis and should be reserved for this purpose, except in those instances in which it has proven superior alone or in combination with other agents, to other forms of therapy, i.e., subacute bacterial endocarditis, brucellosis, tularemia, stubborn urinary-tract infections due to the enterococcus, etc. In general, the severity of toxicity is dependent upon the duration of therapy and total dose employed, the principal toxic effect being damage to the eighth nerve and vestibular apparatus. Streptomycin may give rise to a variety of less severe reactions, including the sensitivity reactions encountered with penicillin. A distinct disadvantage to the use of streptomycin is the frequency and rapidity with which susceptible bacteria develop resistance to the antibiotic.

Dihydrostreptomycin is no longer being employed because of the severe ototoxicity associated with its use.

Define broad-spectrum antibiotics.

The term "broad-spectrum antibiotics" is used to designate certain of the antibiotics that are active against a great variety of microorganisms, in contrast to antibiotics with a narrow spectrum of activity, such as penicillin. Evidence has indicated that the wider the spectrum of activity of an antimicrobial substance, the greater is the toxicity, and the specificity of action is lessened. Fortunately, the now-available broad-spectrum antibiotics are of sufficiently low toxicity to permit their administration in man and are effective in infections caused by gram-positive and gram-negative bacteria, rickettsia, and certain viruses. Because of their pharmacological properties, the broad-spectrum antibiotics, unlike streptomycin, can be administered successfully by mouth. Chloramphenicol, the first of these broad-spectrum antibiotics, has found its chief usefulness against organisms of the *Sal-*

monella group, especially in typhoid fever. Because of the possibility of the development of blood dyscrasias in patients in whom it is employed, it is not recommended for general use. However, it remains a valuable therapeutic agent in selected cases. The tetracycline group of antibiotics is composed of chlortetracycline (Aureomycin), oxytetracycline (Terramycin), tetracycline (Achromycin, Tetracyn, Steclin, Polycycline) and dimethylchlortetracycline (Declomycin). In general, as far as therapeutic effectiveness is concerned, there appears to be little difference among the members of this group, although some differences may exist. For example, dimethylchlortetracycline provides higher and more sustained antibacterial activity in serum than the others, owing to its slower renal excretion. The tetracyclines frequently give rise to gastrointestinal and genitourinary disorders (nausea, vomiting, diarrhea, stomatitis, proctitis, and vaginitis) and can cause staphylococcal pseudomembranous colitis. Erythromycin (Ilotycin, Erythrocin) and novobiocin (Cathomycin, Albamycin) are considered members of the broad spectrum group, although their bacteriostatic action is primarily against gram-positive cocci and they find their chief value in staphylococcal infections, particularly penicillin-resistant strains. There may be mild gastrointestinal upsets following use of these drugs, but, since the fecal flora is unchanged in its content of gram-negative bacilli, yeasts, and clostridia, the chances of staphylococcal enterocolitis developing are unlikely. Indeed, these agents have been effective in the treatment of this disorder which follows use of the tetracyclines. Thus far, the commonest and most troublesome side effects with novobiocin are rashes and drug fever.

What is vancomycin (Vancocin)?

This antibiotic possesses several unique properties: it is bactericidal in readily achieved serum concentrations and is effective against antibiotic-resistant pathogens; there seems to be no cross-resistance between it and other antibiotics; and it averts the development of antibiotic-resistant organisms by quickly destroying the bacteria and maintaining its antibiotic effectiveness. However, the antibiotic must be administered intravenously and may produce thrombophlebitis. Likewise, it may give rise to nausea, chills, fever, and skin rash. Moreover, in view of its potential nephrotoxic properties, it should be used with caution in patients with impaired renal function. Vancomycin is not recommended for routine use, but should be reserved for stubborn infections. In our experience, the antibiotic represents the most potent antimicrobial for the control of hospital-acquired staphylococcic infections.

Define polymyxin and bacitracin.

Polymyxin B sulfate (Aerosporin) is an agent of unique effectiveness in infections due to *Pseudomonas aeruginosa* but of moderate toxicity (renal and central nervous system). This agent is poorly absorbed from the gastrointestinal tract and is therefore administered intramuscularly, 2.5 mg. per kg. of body weight in diluted doses every four to eight hours, not to exceed 200 mg. daily, for cases of pyelonephritis, septicemia, or meningitis due to Pseudomonas that has failed to respond to streptomycin or one of the wide spectrum agents. Oral or topical preparations of polymyxin, alone or in combination with other antimicrobial agents, are of value for the treatment of gastrointestinal disease in which the infection is confined to the intestines, and for ulcers, decubiti, and similar lesions caused by gram-negative bacilli that are accessible for local application (conjunctiva, etc.). Furthermore, this agent is employed prophylactically in intestinal surgery.

Bacitracin for the most part exerts its greatest activity against gram-negative organisms. Since its parenteral administration is often followed by kidney damage and only small amounts are absorbed when given by mouth, this drug finds its chief usefulness as a topical or oral medicament. However, it has proved a valuable agent when given intramuscularly (20,000 to 25,000 units every 6 hours) in selected cases, especially infections caused by stubborn staphylococci.

Give the indications for the use of para-aminosalicylic acid and isoniazid.

PAS (para-aminosalicylic acid) possesses a weak but definite tuberculostatic activity and is effectively employed concomitantly with streptomycin and/or isoniazid to retard the development of resistant organisms. It is usually administered orally, 10 to 12 gm. daily, although it may be used intravenously, in which case the sodium salt is preferred. Except for nausea, anorexia, and diarrhea, there have been few untoward reactions accompanying its use.

Isoniazid (INH, Nydrazid, Cotenozin, Nicomyl) has a high degree of antituberculous activity and is used alone or in combination with PAS and/or streptomycin in the treatment of tuberculosis. It appears that tubercle bacilli develop resistance to isoniazid more rapidly when the drug is administered alone than when it is used in combination. The usual effective dose is 3 to 5 mg. per kg. of body weight, orally, in three divided doses daily. The toxic manifestations of isoniazid seem to be dependent upon the total daily dosage; the chief side reactions are related to the central nervous system—twitching of muscles, restlessness, insomnia, headache, euphoria, and particularly peripheral neuritis.

Discuss combined antimicrobial therapy.

Not infrequently, the physician is confronted with the problem of having at his disposal a number of clinically useful agents, each of which alone is incapable of producing the desired effect in a given case. The temptation to use a combination of antibiotics in such instances is a practical everyday problem. What reliable information is available that will assist the practicing physician in selecting the antibiotics to be used in combination under appropriate indications? Obviously, the most desirable effect to be gained in polyantibiotic therapy is that of synergism, which effect is greater than that to be expected from a simple summation of the independent actions of the several antibiotics employed. Conversely, one of the serious undesirable results of polyantibiotic therapy may be antagonism; the net result may not only be less than the simple additive effect to be expected if the several drugs were to act independently, but less than would result from the effect of either drug used alone. Whereas antibiotic antagonism is conceded at present to have little if any clinical importance, there is not only laboratory but also clinical evidence that polyantibiotic therapy may result in a definite synergistic effect against certain bacteria (such as penicillin and streptomycin in enterococcal infections; streptomycin and either chloramphenicol, oxytetracycline, or chlortetracycline in brucellosis; penicillin and bacitracin in staphylococcal infections; and para-aminosalicylic acid and streptomycin in tuberculosis). Such combinations not only offer increased antibacterial effect, but also may delay the appearance of drug-resistant organisms in certain instances.

Certainly, the status of polyantibiotic therapy in present-day clinical medicine is still largely undetermined, particularly in view of our lack of understanding of the mode of action of these drugs when used in combination. Until these fundamental problems are more fully understood, or until such time as sufficient evidence has been accumulated to indicate which combinations may or may not be useful, the physician can best contribute to the welfare of his patient and to the advancement of knowledge in the field by following certain principles of antimicrobial therapy. Although most infectious diseases are successfully treated without the laboratory establishment of a definite etiological diagnosis, the fact remains that one can employ antibiotic therapy more intelligently if the infecting agent or agents are known. Certainly, those cases failing to respond to therapy deserve the benefit of necessary laboratory studies. One should use doses of single antibiotics that have proved adequate and effective, because in most infections caused by a single organism and in certain types of mixed infections a single agent can be used effectively. For those infections in which the offending organism proves resistant to single drugs by laboratory tests or by adequate therapeutic trial, polyantibiotic therapy should be considered. Where there is already adequate clinical proof that the use of multiple agents may be expected to yield beneficial effects, the proper combination should be employed immediately. In those cases in which clinical evidence of effective combined therapy is lacking, it is necessary to resort to additional laboratory procedures in hope of finding a combination of drugs that will prove more effective than a single agent. Unfortunately, the laboratory has not as yet been able to provide an empirical formula for this purpose. However, it can furnish valuable information that may serve as a guide in the selection of various combinations. Certainly, we are justified in employing antibiotic combinations clinically in those instances in which appropriate tests fail to demonstrate definite antagonism.

List the complications of antibiotic therapy.

(*1*) *Toxic Reactions:* These are due for the most part to the chemical nature of the agent and the effect of these chemicals upon the cellular physiology. The severity of the reactions is often in proportion to the dosage of the drug.

LOCAL: Pain and tenderness at the site of absorption following intramuscular injection; phlebitis with intravenous administration; nausea, vomiting, diarrhea, stomatitis, vaginitis, etc., after oral therapy; chemical meningitis, myelitis, etc., after intrathecal administration; inflammatory reactions when applied topically to certain tissues of the body.

DERMATOLOGIC: Urticarial, erythematous, and eczematoid sensitivity reactions.

SYSTEMIC: Serum sickness and anaphylactoid shock, blood dyscrasias, neurotoxicity, nephritis, periarteritis nodosa, etc.

(*2*) *Development of Drug-Resistant Organisms:* The widespread and indiscriminate use of the antibiotics has resulted in an increased number of drug-resistant bacteria. This microbial resistance after exposure to an antibiotic holds for the antibiotic itself, and also the possibility of the development of cross-resistance to other antibiotics exists. Acquired resistance results, for the most part, from continued exposure to subinhibitory concentrations of these drugs.

(*3*) *Biological Complications:* DEVELOPMENT OF AVITAMINOSIS: The prolonged use of the broad spectrum agents that have an effect on the intestinal flora may impair the production of certain vitamins, especially several members of the B-complex group, and vitamin K, which are elaborated by the bacteria of the lower intestinal tract.

DEVELOPMENT OF SUPERINFECTIONS: Several mechanisms to explain these superinfections have been postulated: (*a*) Administration of an antibiotic results in virtual elimination of susceptible organisms, thus reducing the number competing for available food supply. The resistant organisms then vastly increase in numbers and overwhelm the host's resistance. (*b*) Normal flora supplies certain nutritional requirements of the host. Disturbance of the normal flora results in a nutritional disturbance that modifies the integrity of the mucous membranes, thereby opening a portal of invasion to organisms which normally are unable to penetrate the healthy mucosae. (*c*) Some antibiotics are suspected of directly stimulating growth and virulence of certain organisms.

What is the "gray sickness" syndrome?

This syndrome, which is encountered in premature and other newborn infants receiving chloramphenicol, is characterized by abdominal distention, progressive pallid cyanosis, and vasomotor collapse, often accompanied by irregular respiration. The condition may be fatal if administration of the drug is continued in large doses after the symptoms first appear. The cause is not clear but, as in the kernicterus associated with sulfisoxazole (Gantrisin), it may be due to differences in the manner in which the neonatal infant handles certain drugs.

What is nitrofurantoin (Furadantin)?

This compound is a furan derivative that is rapidly and completely absorbed from the gastrointestinal tract, approximately 40 per cent being excreted in the urine within 4 to 8 hours. Nitrofurantoin possesses a broad antibacterial spectrum that encompasses both gram-positive and gram-negative organisms; its maximum effectiveness is against *E. coli, Staphylococcus aureus, Streptococcus pyogenes,* and *A. aerogenes.* The agent appears to be one of low toxicity. With oral administration in an average daily dose of 2.2 to 3.6 mg. per pound (5 to 8 mg. per kg.) of body weight in divided doses 4 times daily, nausea, vomiting, headache, and dizziness are encountered in an occasional patient. Cutaneous and febrile reactions suggesting the development of hypersensitivity to the drug have also been observed in a few instances. Thus, nitrofurantoin appears to be a relatively safe and effective urinary antiseptic.

What factors influence the effectiveness of mandelamine as a urinary antiseptic?

Mandelamine (methenamine mandelate) is a chemical combination of mandelic acid and methenamine, which is readily absorbed from the gastrointestinal tract and rapidly excreted into the urine. Susceptible organisms include *E. coli, Staphylococcus aureus,* and certain streptococci. Its antibacterial effectiveness in urine is largely dependent upon its concentration and the maintaining of an acid medium. Although the compound itself acidifies the urine, an acidifying agent should be employed, especially in the treatment of infections caused by organisms that form ammonia.

Discuss the prophylactic and therapeutic usefulness of nystatin (Mycostatin) in moniliasis.

Clinically, it is well known that the overgrowth of *Candida albicans* in the gastrointestinal tract is associated with the prolonged use of antibiotics, particularly the broad-spectrum agents. Likewise, it has been shown experimentally both that this overgrowth occurs with greater frequency and that the invasiveness of *Candida* is apparently increased following administration of antibiotics. Recent studies have indicated that nystatin (Mycostatin) is highly effective against certain types of monilial infections, namely, oral and vaginal moniliasis. In addition, controlled studies have shown that the increase of yeast in the feces was significantly less after administration of the combined drugs (i.e., tetracycline and nystatin) than when a broad-spectrum antibiotic was given alone. Thus, it would seem practical to employ nystatin prophylactically, when a broad-spectrum antibiotic is used, particularly in those conditions that seem to favor the development of monilial infections, for example, in debilitated patients, the concurrent use of cortisone and related compounds in diabetic patients, in pregnant women, and in patients requiring long-term therapy. Therapeutically, nystatin is used orally and/or locally in cases of gastrointestinal and genitourinary moniliasis complicating antibiotic therapy. In addition, it may be used in pulmonary moniliasis, although the results are far less striking.

In what diseases is amphotericin B (Fungizone) useful?

Amphotericin B appears to be the first broad-spectrum antifungal agent available for satisfactory clinical use in the treatment of deep mycotic infections, especially North American blastomycosis, histoplasmosis, and cryptococcosis (torulosis). The drug is least effective in systemic coccidioidomycosis and candidiasis (moniliasis) but worthy of trial in the absence of other effective chemotherapy.

What are the desirable properties of a fungicide for superficial mycotic infections?

(1) The compound must be fungistatic or, preferably, fungicidal. (2) Bactericidal activity is highly desirable, because fungous infections are frequently complicated by secondary bacterial infections. (3) The agent must be capable of penetrating the stratum corneum and coming in contact with the fungi that are embedded there. (4) The active drug and the vehicle should be neither irritating to the tissue nor capable of producing sensitization. Although many highly active fungicides have been developed, the fatty acid fungicides present most of the above features (undecylenic acid [Desenex], propionic acid [propionate compound], and caprylic acid [caprylic compound]).

What is griseofulvin (Fulvicin, Grifulvin, Griseo-Fulvin)?

Griseofulvin is a new antifungal antibiotic that effectively inhibits the three genera that produce most superficial fungous infections. These are the microsporum group, which is the chief cause of tinea capitis; the trichophyton group, which causes tinea pedis, tinea corporis, tinea ungium, and sometimes tinea capitis; and epidermophyton, which may cause tinea cruris and tinea pedis. The antibiotic is absorbed from the gastrointestinal tract and deposited in the keratin of the skin, hair, and nails. Griseofulvin is fungistatic and inhibits the growth of susceptible fungi, especially the growing tips of the terminal hyphae but they remain viable within the infected tissues. Hence, treatment with the drug must be continued until infected hairs, skin areas, or nails are removed, either by natural processes or artificial measures.

Discuss the role of oxidizing agents as antiseptic drugs.

A number of antiseptic drugs exert antibacterial action because of their oxidizing properties. The important members of this group include potassium permanganate, sodium perborate, hydrogen peroxide, and the metallic peroxides, which exert a germicidal action by oxidizing susceptible constituents of the protoplasm of bacteria, presumably enzyme systems active in the reduced form, with the release of nascent oxygen. The second group includes the halogens, chlorine and iodine. The exact manner by which iodine exerts its antibacterial effect is unknown. However, chlorine exerts this action in the form of undissociated hypochlorous acid, which oxidizes certain enzyme systems essential to bacterial metabolism.

Give the mechanism of the amebicidal action of emetine.

Emetine has a direct lethal action on *E. histolytica* in that, experimentally, it causes degeneration of the nucleus and reticulation of the cytoplasm, which interferes with the multiplication of trophozoites, eventually leading to the eradication of the parasites. Despite the apparent high amebicidal activity, emetine is not recommended for the routine treatment of intestinal amebiasis, in that it cures only about 15 per cent of patients, fails to eradicate cysts, and may give rise to a variety of toxic manifestations (vomiting, diarrhea, dizziness, myositis, peripheral neuritis, hypotension, tachycardia, precordial pain, dyspnea, and electrocardiographic abnormalities such as flattening and inversion of T waves and prolongation of A-V conduction). These untoward reactions may occur with any dose level of emetine, depending on individual susceptibility to the drug. Despite the above, emetine is used in patients with severe amebic dysentery, amebic abscesses, and amebic hepatitis, although chloroquine (Aralen) is equally effective in extraintestinal amebiasis and is much less toxic than emetine. The two drugs may be used alternately but not at the same time.

Outline the principles of specific therapy for amebiasis.

The various therapeutic agents for amebiasis differ in their usefulness depending upon:

(*1*) *Amebicidal Effectiveness:* Such drugs as emetine, chloroquine (Aralen), carbarsone, chiniofon, iodochlorhydroxyquin (Vioform), diiodohydroxyquin (Diodoquin), fumagillin (Fumidil), bacitracin, paromomycin (Humatin), and the tetracyclines all possess activity against *E. histolytica.*

(*2*) *Effect upon the Bacterial Flora of the Colon:* Bacterial associates are required for the growth of *E. histolytica,* and secondary bacterial infections are often associated with amebiasis. Since the amebicidal drugs (except the tetracyclines) do not effect bacteria, it is often necessary to prescribe therapy such as the sulfonamides or one of the tetracycline group of drugs to alter the bacterial flora or to eradicate secondary infections.

(*3*) *The Character of the Amebic Infection:* Amebiasis limited to the intestinal tract can be successfully treated with any one of the above agents (except emetine and chloroquine [Aralen]), whereas extraintestinal amebiasis (amebic abscess, hepatitis) is best treated with emetine or chloroquine (Aralen).

Discuss the uses of formaldehyde solution (formalin).

Formaldehyde, in proper concentration, is an effective germicide against all forms of organisms, but it is too irritating to be applied to body tissues in effective concentrations. Hence, its widest use is in the disinfection of surgical instruments, human excreta, etc. In addition, formaldehyde is capable of converting toxins to toxoids, by virtue of its detoxifying properties, and is of value in the preparation of nontoxic antigens, such as diphtheria toxoid.

Of what clinical value are glycol vapors?

Glycol vapors are toxic to bacteria, viruses, and fungi. Since the glycol vapors are highly water soluble, they dissolve in the aqueous droplets in which air-borne bacteria are transported and herein attain bactericidal concentration. Clinically, glycol vapors have been shown to reduce the number of bacteria in the air, and some workers have claimed a reduction in the incidence of air-borne infections with this procedure.

Give the indications and contraindications for the use of aspidium (male fern).

Aspidium is a useful drug for ridding the intestinal tract of tapeworms (cestodes), especially *Taenia saginata* (beef) and *Dibothyriocephalus latus* (fish), in that it paralyzes the muscle of the parasite and the worm can then be removed by a cathartic. Since aspidium is an irritant, it causes nausea, vomiting, and diarrhea when given undiluted and in high doses; it stimulates the central nervous system with resulting tremors that may progress to convulsions and respiratory failure, as well as depress cardiac function. Hence, it should never be used in weak or emaciated patients, in persons with gastrointestinal ulceration, or with diseases involving the heart, liver, or kidney, nor in pregnancy.

For which metazoan infections are the following employed? (1) Quinocrine hydrochloride (Atabrine), (2) hexylresorcinol (Caprokol), (3) piperazine (Antepar), and (4) tetrachlorethylene.

(1) Atabrine: cestodiasis (tapeworm); (2) Caprokol: trichuriasis (whipworm); (3) Antepar: ascariasis (roundworm), enterobiasis (pinworm, seatworm); (4) tetrachlorethylene: uncinariasis (hookworm).

For which parasitic diseases are the following employed: (1) santonin, (2) hexylresorcinol, and (3) piperazine?

(1) Santonin: *Ascaris lumbricoides* (roundworm); (2) hexylresorcinol: *Necator americanus* (hookworm), *Ascaris lumbricoides* (roundworm), *Oxy-*

uris vermicularis (pinworm), *Hymenolepis nana* (dwarf tapeworm), and *Trichuris trichuria* (whipworm); (3) piperazine: *Ascaris lumbricoides* (roundworm) and *Oxyuris vermicularis* (pinworm).

Describe the action of chlorophenothane (DDT) in arthropods and its therapeutic applications in man.

The primary site of lethal action of DDT in arthropods is the nervous tissue, especially the peripheral nervous system. DDT (10 per cent powder or diluent) is effective in the treatment of pediculosis. However, it should not be employed alone for the treatment of scabies, as DDT is not an effective miticide.

Give the properties of methylrosaniline chloride (gentian violet).

Gentian violet is a member of the triphenylmethane or rosaniline group of dyes which possesses activity against the gram-positive organisms, especially staphylococci, *C. diphtheriae* and *Ps. aeruginosa;* many species of *Monilia, Trichophyton,* and *Torula;* the causative organism of Vincent's angina; and *Strongyloides* and *Oxyuris* infestations. Clinically, it has its main usefulness in the form of methylrosaniline chloride solution (gentian violet solution), or carbolfuchsin paint (Carfusin) for local or topical administration. For oral therapy, enteric-coated tablets are employed.

Describe the anti-infective action of sulfur.

The chief usefulness of sulfur is in the treatment of certain skin disorders. Although its antibacterial action is feeble, it possesses keratolytic properties and is a valuable parasiticide as well. Sulfur is employed as an ointment (sulfur ointment U.S.P.). On occasion it may produce a characteristic dermatitis venenata.

Define surface-active agents.

The surface-active agents are widely used as wetting agents, detergents, and emulsifiers, and, because of their ability to precipitate or denature protein or form complexes with it, they destroy or inactivate microorganisms. Of this group, only the cationic agents are employed as germicides, such as benzalkonium chloride (Zephiran chloride). They are relatively nonirritating to tissues. They wet and penetrate tissue surfaces and possess detergent, keratolytic, and emulsifying actions. They have a rapid onset of bactericidal action to a wide variety of gram-positive and gram-negative organisms but cannot be relied upon to kill spores. Their activity is antagonized by soaps. Benzalkonium chloride is widely used as a disinfectant on unbroken or denuded skin, in deep lacerations, for irrigation of the eyes, bladder, vagina, etc. Since surface-active agents are detergents as well as bactericides, they have found wide usefulness in the field of sanitation (milk cans, dairy machinery, food-processing machines), as well as for many other domestic cleaning purposes (dishes, etc.).

Define and give treatment for pediculosis capitis.

A louse infestation producing an irritating roseate papular dermatitis of the head. Treatment consists of cutting the hair short, thorough washing of hair and scalp, working 1 ounce of Kwell lotion (1 per cent gamma benzene hexachloride) into the hair and scalp, placing a covering cap on the head for 12 hours, at the end of which time a second application of lotion is made. On the next day, the hair is again thoroughly washed and combed. Re-examination of patient should be made one week later, and, if any evidence of infection is present, the treatment should be repeated.

Discuss the problems related to and the treatment for scabies (sarcoptic itch).

Scabies continues to be a problem, especially in poorly managed institutions and in overcrowded areas with substandard living conditions. Treatment consists of a hot soapy bath (all crusts should be removed), followed by Kwell ointment (1 per cent gamma benzene hexachloride) 1 ounce applied to entire body below the neckline. Twelve hours later another application of ointment, followed in another twelve hours by a second bath. Clean garments are then worn, and all previous wearing apparel should be dry cleaned or laundered.

Give the mode of action of trypsin (Tryptar) and chymotrypsin (Chymar).

Blood clots and pus are liquefied and fibrin deposits and necrotic tissue are digested by these agents. Living tissue is not affected because there are both specific and nonspecific trypsin inhibitors in serum.

THERAPEUTIC AGENTS IN NEOPLASTIC DISEASES

Compare chemotherapy of infections and neoplastic diseases.

Although the basic problem in the chemotherapy of neoplastic disease is in a broad sense similar to that of infectious disease, certain fundamental differences do exist between the two. (1) In microbial disease the offending agent is foreign to the host, whereas malignant cells cannot be considered "foreign." (2) The biological requirements of the infectious invader's cells are sufficiently different from those of the host as to be susceptible to differential attack by antimicrobial agents, whereas the biological requirements for growth and multiplication are qualitatively indistinguishable between malignant and normal cells. (3) The causative agent in infectious diseases is vulnerable to the various body defense mechanisms which aid the specific antimicrobial agents greatly, whereas malignant cells appear to be invulnerable to the defense mechanism of the host.

Evaluate the present status of chemotherapy of neoplastic diseases.

At this time no curative chemical agent for neoplastic disease is available, although various drugs and hormones are available that can induce temporary remissions. Such are the cytotoxic agents which exert their action by virtue of their chemical (polyfunctional alkylating agents, folic acid analogs, etc.) or physical (radioactive isotopes) properties and agents which exert their action by altering the environment of the cancer cell (hormones such as estrogens, androgens, adrenocortical steroids). In addition, the hormones, particularly the androgens (because of the anabolic effect) and adrenocortical steroids (because of their ability to alter the response of tissues to injury), are of value in that they appear to support the host against the ravages of malignant disease.

Discuss the cytotoxic action of mechlorethamine (Mustargen) and triethylene melamine (TEM).

The most important pharmacological actions of the polyfunctional alkylating agents, of which group mechlorethamine and triethylene melamine are important members, are the cytotoxic reactions that follow the administration of sublethal doses. The alkylating agents inhibit mitosis and cell division in all germinal tissues (bone marrow, lymphoid tissue, etc.), and the proliferating cells show cytological evidence of altered chromosomal structure and function. These changes, which take place in the bone marrow and lymphoid tissue, are reflected in the formed elements of the circulating blood, i.e., lymphocytopenia, granulocytopenia, thrombocytopenia, and fall in red blood-cell count. In certain neoplastic tissues (malignant lymphomas, undifferentiated bronchogenic carcinoma), this activity of the alkylating agents is that of inhibiting the proliferative activity and thereby causing regressive changes.

Of what value is 6-mercaptopurine (Purinethol)?

6-Mercaptopurine, an antimetabolite of adenine and hypoxanthine, interferes with nucleic acid metabolism. Its chief action is on bone marrow (hypoplasia) and on intestinal epithelium (denudation of surface epithelium, etc., which gives rise to nausea, vomiting, and diarrhea). The chief value of this compound is in bringing about remissions in patients, particularly in children, suffering with acute leukemia.

Discuss the biologic effect of radiation produced by radium, roentgen rays, radioactive substances and atomic factors.

The biological effect of these forms of radiation is produced when, impinging upon living tissue, the energy initiates a temporary separation of atoms and molecules into electrically charged particles (i.e., ionization), and the release of energy as chemical change or heat. The effects are proportional to the amount of ionization produced and depend on the tissue affected. Any living cell can be destroyed by sufficiently large doses of radiation, but cells differ in their susceptibility and resistance. The exact mechanism involved with the metabolic upheaval induced by high energy radiation is unknown, but most emphasis has been given to the inhibition or destruction of enzyme systems, especially to sulfhydryl-obligate enzymes, which are very radiosensitive.

What is meant by the "half-life" of radioactive elements?

A radioactive element is one that gives off ionizing energy because of a spontaneous internal rearrangement of the nucleus. Radium normally is unstable; therefore, it undergoes rearrangement constantly. Phosphorus, iodine, sodium, and other elements with stable nuclei can be made radioactive by processes of neutron or deuteron bombardment in a cyclotron or nuclear chain reactor. The speed of nuclear rearrangement varies between different elements and different isotopes of the same element. In order to express this feature, the "half-life" of the radioactive elements is calculated. The half-life is the time taken by the element in losing one half of its radioactivity exponentially. The half-life of the radioactive elements varies from a fraction of a second to thousands of years. The radioactive isotopes that have been of greatest therapeutic interest are those with a half-life of a few days or weeks; those with suitable type and energy of radiation; those with availability in good yield from established cyclotrons or chain reactors.

Give the "half-life" and usefulness of: (1) phosphorus-32 (p^{32}), (2) radiogold (Au^{198}) colloid, and (3) cobalt-60 (Co^{60}).

(1) Phosphorus (P^{32}) has a half-life of 14.3 days and emits moderately powerful beta radiation. It concentrates in bone marrow and lymphoid tissue and is the agent of choice in polycythemia. In chronic myelocytic leukemia P^{32} is as effective as x-rays and avoids the radiation sickness of the latter. (2) Radiogold (Au^{198}) colloid emits beta and gamma radiations and has a half-life of 2.7 days. It is injected into peritoneal or pleural cavities in the palliative treatment of effusions associated with metastatic malignant tumors. (3) Cobalt-60 (Co^{60}) has a half-life of 5.3 years and emits a very penetrating gamma ray equivalent to that from a 2.5 million volt x-ray machine. It has been used for both external and interstitial radiation.

Discuss the action of the folic acid analogs.

Studies in human nutrition and microbiology have demonstrated the fundamental importance of pteroylglutamic acid (folic acid) in cellular metabolism. The folic acid analogs are important in that certain of them block the important actions of folic acid in nucleic acid metabolism. This antimetabolic effect on folic acid has been demonstrated by inhibiting the growth of microorganisms, which require folic acid for growth, by means of low concentrations of the antagonist; on the addition of folic acid, the inhibition is reversed. Also, the signs and symptoms associated with poisoning by the antagonists are similar to those of an absolute folic acid deficiency. Clinically, the application of the action of the folic acid antagonists, particularly 4-amino-N^{10}-methylpteroylglutamic acid (amethopterin, Methotrexate), is made in the treatment of acute leukemia.

Discuss the clinical applications of radioactive isotopes.

Radioactive isotopes are useful in clinical medicine as diagnostic aids (for evaluation of thyroid function, localization of tumors), for physiological determinations (measurement of the volume of fluid compartments of the body and total red blood-cell volume, for studies of circulatory status, etc.), and as therapeutic agents (hyperthyroidism, metastatic carcinoma of the thyroid, neoplasms of bone marrow, etc.).

HORMONAL AGENTS

Differentiate between natural, artificial, and synthetic hormones.

Natural hormones are those normally found in nature, in contrast to artificial substances producing similar effects, although there may be some quantitative or even qualitative differences between their actions. Certain natural hormones have been synthesized and are available as synthetic preparations, but the term "synthetic hormone" cannot be used as a synonym for "artificial hormone."

Discuss the mode of action of the aryl sulfonylureas in diabetes mellitus.

There is a good deal of conflicting evidence on the hypoglycemic action of the aryl sulfonylureas, tolbutamide (Orinase) and chlorpropamide (Diabinese), in diabetes mellitus. However, some facts are established. The drugs do not influence the alimentary absorption of glucose or reduce the renal threshold for it, nor do they accelerate glycolysis in the blood. They do not affect endocrine glands other than the pancreas and they do not directly affect peripheral utilization of glucose. It is agreed by some workers that the initial hypoglycemic response is probably due to stimulation of pancreatic beta-cell production of insulin. Likewise, there is pretty clear evidence that the sulfonylureas do not promote the uptake of glucose from the blood by extrahepatic tissues or potentiate in any way the peripheral action of endogenous insulin, but there is a suppression of glucose release by the liver. Whether this latter effect is due merely to the additional insulin released, or is evidence of direct sulfonylurea action upon the liver, has not been established.

List the most important known actions of insulin.

(1) Acceleration of glucose oxidation, (2) acceleration of conversion of glucose to fat, (3) increase in liver glycogen formation and/or inhibition of hepatic glycogenolysis by other hormones, (4) inhibition of glyconeogenesis of liver, and (5) inhibition of excessive ketogenesis.

What is the advantage of employing insulin mixtures?

If insulin injection and protamine zinc insulin injection are mixed in the syringe immediately before use, the combined actions of the resulting mixture will differ from those of the two preparations if injected separately. This is because the protamine in protamine zinc insulin injection is capable of reacting with a certain amount of additional regular insulin, establishing a new equilibrium. Mixtures in which the ratio of regular to protamine is less than 2:1 possess essentially the properties of protamine zinc insulin (onset 6 to 8 hours, period of maximum action 12 to 24 hours, and duration of action 48 to 72 hours); a 2:1 mixture behaves essentially like isophane insulin injection (NPH-50) (onset 2 hours, period of maximum action 10 to 20 hours, and duration of action 28 to 30 hours); and a 3:1 mixture behaves like globin zinc insulin (onset 2 to 4 hours, period of maximum action 8 to 16 hours and duration of action 16 to 24 hours). The chief advantage of insulin mixtures is that any mixture can be prescribed to meet the individual need of the patient. However, the mixtures are unstable and therefore must be prepared just before use.

Discuss the dietary factors influencing the dose of insulin.

The diet of a diabetic patient must contain an adequate amount of calories, protein, minerals and vitamins but can vary widely with respect to the proportion of calories provided by fat and carbohydrates. In a mild diabetic who has a fair carbohydrate tolerance, it is possible to keep the urine glucose-free by a low carbohydrate and high fat intake, although the limits of such a dietary regimen are set by the distastefulness of a low carbohydrate diet and the degree of ketosis that develops. In the more severe cases, a more liberal carbohydrate intake is allowed, and proper combustion is assured by the administration of sufficient exogenous insulin. Since an increase in carbohydrates does not require a proportionate increase in insulin, many diabetics enjoy a liberal carbohydrate diet properly controlled by only a little more insulin than was required with a more rigidly restricted diet.

Give the preparations and indications for therapy with thyroid hormone preparations.

Two thyroid hormone preparations are available—desiccated thyroid gland (thyroid), which contains approximately 20 per cent iodine, and thyroxine (thyroxin), which contains 64 per cent iodine. The former is more readily and completely absorbed after oral ingestion, but the latter can be used parenterally. Recently, triiodothyronine (Cytomel, Trionine), an active principle of the thyroid gland, has been employed in cases of myxedema. Its activity was compared to that of thyroxine, the other active principle, and it was found that the over-all calorigenic action of the two drugs was similar, but, on the basis of minimal effective doses, triiodothyronine was five times more active. However, its role in the management of thyroid deficiency states is unsettled.

The specific indications for the therapeutic use of thyroid preparations are myxedema and cretinism. In addition, thyroid is also used to advantage in certain conditions that are not characterized by a primary thyroid deficiency, but have low metabolic levels unassociated with myxedema—namely, sterility and habitual abortion, arthritis, etc. In general, the thyroprivic individual reacts more dramatically to a small amount of thyroid hormone than an individual who is not suffering from myxedema. Thus, the response to therapy is often of significance as to the regulation of dosage. Not infrequently, excessive amounts of thyroid hormone are employed in hope of obtaining the desired effect.

Discuss the mechanism of action of the various antithyroid drugs.

In general, an antithyroid drug is a chemical agent that lowers the basal metabolic rate by interfering with the synthesis, release, or peripheral action of the thyroid hormone. (1) *The goitrogens* (thiouracil, propylthiouracil, methylthiouracil) suppress the formation of thyroxine and triiodothyronine (the active principles of the thyroid gland). These antithyroid drugs are employed in the medical treatment of hyperthyroidism in Graves' disease and toxic nodular goiter, preoperatively, and as an ancillary measure in the treatment of disease other than that of the thyroid, such as the anginal syndrome (although radioactive iodine is now being advocated in this condition). (2) *Iodine* probably exerts its therapeutic effect by promoting colloid storage and involution of the thyroid gland. Iodine finds its chief usefulness in the treatment of thyrotoxicosis prior to thyroidectomy. It is best added to the therapeutic regimen after the basal metabolic rate has been brought to within the limits of normal with one of the goitrogens, preferably propylthiouracil, since it represents the least toxic preparation. (3) *Radioactive iodine* (I^{131}), like iodine, is deposited in the colloid of the follicle and the destructive beta rays act upon the parenchymal cells of the thyroid; the extent of damage is dependent upon the dosage of the isotope. I^{131} is useful in the treatment of hyperthyroidism and thyroid neoplasia.

Compare the physiologic effects of oxytocin and ergonovine.

Oxytocin and ergonovine are the oxytocic fractions of posterior pituitary extract and of ergot respectively. Both stimulate powerful contractions of the musculature of the uterus at or near term, in labor, and following delivery or abortion. They produce only mild contractions in the myometrium of the nonpregnant uterus and stimulate it with gradually increasing effectiveness as pregnancy begins and progresses toward term. The oxytocic effect is also modified by the route of administration and the dosage in which the preparations are employed. Ergonovine is effective orally, but oxytocin is not. Both are effective by the intramuscular and intravenous routes; contraction of the uterine muscle is prompter and much more forceful when the latter route is employed. When used in small dosage, oxytocin augments or develops normal uterine contractions that are followed by a normal period of muscular relaxation. With larger dosages, uterine tone increases and contractions become stronger; when even larger amounts of the drugs are used, the uterine muscle contracts tetanically and all evidence of intermittent contractions is lost. The effects of ergonovine on uterine musculature are similar to those of oxytocin, but in the dosages usually employed in obstetrics the effects of increased uterine tone and muscle spasm overshadow the effect of augmentation of contractions of a normal type. Finally, the action of ergonovine is a more prolonged one than that of oxytocin.

At present, there is insufficient published data from which to report with certainty the exact extragenital effects of oxytocin, which has been synthesized in its pure form but relatively recently. Oxytocin does affect the breasts and initiates the so-called "let down" reflex during lactation. Commercial preparations of it in clinical use contain about 10 per cent of the pressor factor of posterior pituitary extract. Pure oxytocin is said to lower blood pressure. The clinical preparations tend, however, to raise pressure, particularly in patients who exhibit latent or established hypertension. This effect is probably the result of the contaminant pressor factor. Furthermore, the vasopressor factor in commercial oxytocin may produce dangerous coronary artery spasm. When it is given to a patient anesthetized with a general anesthetic agent that may cause cardiac irritability, such as cyclopropane, a disaster—severe shock or death—may result. Ergonovine, however, is not free of side effects on the blood pressure. It contains a mild vasopressor factor that, in certain patients, particularly those with existing or latent hypertension, increases blood pressure. The vasopressor effect of both preparations is occasionally striking and may reach a severity that is dangerous. It is more frequently encountered with oxytocin than with ergonovine and is least frequently encountered with the semisynthetic preparation, methylergonovine, which, in general, has the same attributes of ergonovine.

Discuss the value of hypophysectomy in the treatment of malignant tumors.

It is generally accepted that estrogens and androgens are in many instances associated with the growth of cancer of the breast and prostate. This view is based on the remissions obtained in such cases by sex hormone control, such as elimination of estrogens or androgens from the body. For such control, castration or/and adrenalectomy have been used with good results. On the other hand, there is clinical evidence which suggests that pituitary hormones influence the growth of these malignancies by routes other than by way of the steroid hormones. For these reasons, hypophysectomy is a rational approach in the treatment of metastatic cancer of breast and prostate. Complete removal of the pituitary tissue is followed by cessation of secretion of the pituitary hormones and, as a result, also of steroid hormones. Thus, by a single operation, complete control of pituitary and sex hormones is achieved. Preliminary reports indicate that the results obtained in metastatic cancer of the breast with hypophysectomy are at least as good as other forms of endocrine treatment of this malignancy.

Give a classification of diseases suitable for steroid therapy.

(1) Acute diseases, possibly fatal or with potentiality of severe structural damage—fulminating rheumatic fever, intractable status asthmaticus, disseminated lupus erythematosus, Waterhouse-Friderichsen syndrome, tuberculous meningitis, etc. (2) Acute, self-limited, and ordinarily non-fatal diseases—penicillin reactions, gout, brucellosis, typhoid fever, viral hepatitis, seasonal asthma, ocular disturbances, etc. (3) Chronic diseases, that carry some risk of premature fatal termination during an acute exacerbation, such as acquired hemolytic anemia during an acute hemolytic crisis. (4) Chronic, but ordinarily not fatal diseases—rheumatoid arthritis, dermatomyositis, ulcerative colitis, etc.

List the commonly employed adrenal glucocorticoids and give the average initial dosage of each.

Cortisone acetate (Cortone, Cortogen), 75 mg. every 8 hours; hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone), 60 mg. every 8 hours; prednisone (Deltra, Deltasone, Meticorten, Paracort), 10 mg. every 8 hours; prednisolone (Delta-Cortef, Hydelta, Meticortilone, Meti-Derm, Paracortol), 10 mg. every 8 hours; triamcinolone (Aristocort, Kenacort), 4 mg. every 8 hours; methylprednisolone (Medrol), 4 mg. every 8 hours; and, dexamethasone (Decadron, Deronil, Gammacorten), 0.75 mg. every 8 hours.

Discuss the use of adrenocortical steroids in infectious diseases.

Since these compounds inhibit inflammatory processes, infection may develop during the course of steroid therapy without the usual signs and symptoms. Hence, the importance of careful observation in patients receiving prolonged treatment with these anti-inflammatory compounds, so that appropriate antimicrobial agents may be promptly started. Since a state of relative adrenal insufficiency usually develops during long-term hormonal therapy, the adrenocortical steroids should be continued or increased during the period of added stress caused by the infection. Likewise, in infections accompanied by acute, shocklike reactions and/or hyperpyrexia that may prove fatal (e.g., typhoid fever, meningococcemia, brucellosis, etc.), the hormones may be used as adjuvant therapy, especially in the early stages of the disease process. In general, the use of adrenocortical steroids in infectious diseases should be limited to those conditions in which the bacterial infection is susceptible to antimicrobial therapy.

Discuss the untoward reactions following the administration of adrenocortical steroids.

For the most part, the untoward reactions associated with steroid therapy are manifestations of a state of hypercorticism. (1) Disturbances in electrolyte metabolism, especially sodium retention and potassium loss, occur in a certain number of patients. However, the parent steroids are more likely to produce these changes than are prednisone and prednisolone. In fact, this seems to be the major advantage of these newer compounds. (2) Mild elevation of blood pressure, especially with ACTH and in patients with renal insufficiency or preexisting hypertension. (3) Psychiatric changes ranging from simple euphoria to severe psychotic episodes (particularly in patients with history of prior mental instability). Convulsive seizures may also occur, especially in children. (4) Diabetics usually develop increases in glycosuria and hyperglycemia, but rarely do patients develop diabetes mellitus ("steroid diabetes") during adrenocortical therapy. It is believed that these patients had a predisposition to diabetes before therapy started. (5) Osteoporosis may follow or be aggravated with subsequent pathological fracture following long-term steroid therapy, especially in patients with rheumatoid arthritis and in postmenopausal women. (6) Peptic ulcers may develop and, in some, perforation occurs without warning. (7) Induced hypercorticism alters tissue reaction to injury, infection, and toxemia. (8) Acne, hirsutism, menstrual disturbances, "moon face," "buffalo hump," striae, and other changes may follow prolonged adrenocortical therapy.

Outline the prophylactic measures employed when cortisone therapy is discontinued.

When cortisone therapy is discontinued, the endogenous secretion may not be adequate for several days and varying degrees of hypocorticism (muscular weakness, mild hypoglycemia, fall in blood pressure, or more severe manifestations of adrenal insufficiency) may ensue. This situation may occur, since the secretion of ACTH is suppressed during the administration of cortisone and the adrenal glands atrophy. Therefore, during the period of cortisone withdrawal, the patient should receive moderate doses of ACTH.

List the contraindications for adrenocortical therapy.

In general, the steroids should not be used in the presence of active or questionably healed tuberculosis, peptic ulcer, diabetes mellitus, diminished cardiac reserve, hypertension, psychotic tendencies, and renal insufficiency. However, as with other powerful therapeutic agents, the advantages of hormonal therapy must be weighed against possible deleterious effects. For example, steroid substance therapy is indicated in patients with Addison's disease and active tuberculosis.

Section 5

CLINICAL PATHOLOGY

HEMATOLOGY

Define (1) hemoglobinemia, (2) hyperchromemia, and (3) oligochromemia. List several diseases in which these may be observed.

(1) Appearance of hemoglobin in plasma as a result of excessive erythrocyte destruction; frequently observed in acute infectious diseases, acquired and congenital hemolytic anemias, hemolytic reactions following transfusion, severe burns, and chemical poisoning. (2) Usually an apparent rather than a real increase in hemoglobin concentration; cardiac disease with cyanosis, erythremia or "idiopathic polycythemia," and severe diarrhea of cholera. (3) Decrease in hemoglobin concentration; the degree of decrease may be slight (mild secondary anemia) or very marked (pernicious anemia, leukemia, or hookworm infestation).

Enumerate the hematologic indexes based on erythrocyte size and hemoglobin concentration which are most useful in the classification of anemias.

(1) Mean corpuscular volume (M.C.V.) = 87 ± 5 cubic microns.

(2) Mean corpuscular hemoglobin (M.C.H.) = 29 ± 2 micromicrograms (gamma gamma).

(3) Mean corpuscular hemoglobin concentration (M.C.H.C.) = 34 ± 2 per cent.

List and give the normal values for the laboratory studies on peripheral blood which must be performed in order to permit calculation of the above indexes.

(1) Erythrocyte count: female 4.8 ± 0.6 millions/cu. mm.; male 5.4 ± 0.8 millions/cu. mm.

(2) Hemoglobin: female 14.0 ± 2.0 gm./100 ml.; male 16.0 ± 2.0 gm./100 ml.

(3) Hematocrit: female 42.0 ± 5.0 per cent; male 47.0 ± 7.0 per cent.

In what conditions is the fragility of erythrocytes apt to be (1) normal, (2) increased?

(1) Purpura and secondary and pernicious anemia. (2) Hemophilia and chronic obstructive jaundice.

What are the laboratory findings in thrombocytopenic purpura haemorrhagica? In hemophilia?

Purpura: Decreased number of blood platelets, increased bleeding time, normal clotting time, nonretractile clot, capillary resistance test positive.

Hemophilia: Normal number of platelets, bleeding time normal, clotting time increased, capillary resistance test negative.

What is sludged blood?

In the healthy person circulating red cells in small vessels show no tendency to adhere to each other or to the inner surfaces of the walls. The blood flow, with a central axial stream, is controlled in rate by the contracted vessels, the arterioles. The shapes and sizes of the vessels of the peripheral vascular bed are such as to form a variable bottleneck in the circulatory system. In a wide variety of infections, shock, and other conditions, the blood cells may agglutinate into masses (sludge) that slow the rate of blood flow in small vessels and temporarily or permanently plug small arterioles. Anoxic effects result in vascular endothelium and visceral tissues. Agglutinated red cells tend to be ingested and destroyed by the phagocytic cells of the spleen and liver. There appears to be a close correlation between the degree of blood-sludge formation and the erythrocyte sedimentation rate.

Of what value is the determination of the sedimentation rate of the erythrocytes?

Any *acceleration* of the sedimentation rate is indicative of tissue destruction, as in an infectious process or carcinoma. It is valuable in determining the activity of tuberculous and rheumatic processes, myocardial infarctions, and pelvic infections. The rate is also increased in pregnancy, anemia, intoxications, and endocrine diseases.

The rate is *retarded* or unaffected in severe cachexia, erythrocytosis, anaphylaxis, and disease of the liver.

What diseases are characterized by (1) eosinophilia, (2) monocytosis?

(*1*) *Eosinophilia:* May be associated with:

ALLERGY: Angioneurotic edema, asthma, eczema, pollenosis or urticaria.

SKIN DISEASES: Dermatitis herpetiformis, erythema multiforme, herpes zoster, pemphigus, psorias.

PARASITES: Most marked with those that invade tissues—*E. histolytica, Echinococcus, Filaria, Schistosoma, Trichina;* less marked with intestinal parasites such as *Ascaris, Taenia,* or *Uncinaria.*

HEMATOPOIETIC-SYSTEM DISEASES: Eosinophilic leukemia, granulocytic leukemia, Hodgkin's disease, pernicious anemia; after splenectomy.

WITH CERTAIN INFECTIONS: Chorea, coccidioidomycosis, gonorrhea, scarlet fever, active tuberculosis; after certain infections such as measles, pneumonia, and varicella.

WITH NEOPLASMS: Those involving serous surfaces or bone, or with tissue necrosis.

MISCELLANEOUS: Adrenal cortical hypofunction (Addison's disease); after certain chemicals—camphor, phosphorus, pilocarpine or raw liver; after irradiation; in familial eosinophilia; Loeffler's syndrome, periarteritis nodosa, and other collagen vascular diseases; sarcoidosis; tropical eosinophilia.

(*2*) *Monocytosis:* May be present with:

BACTERIAL INFECTIONS: Brucellosis, subacute bacterial endocarditis, tuberculosis, typhus; occasionally, typhoid.

PARASITIC DISEASES: Cutaneous leishmaniasis (oriental sore), kala-azar, malaria, Rocky Mountain spotted fever, trypanosomiasis.

MONOCYTIC LEUKEMIA: Occasionally seen with Hodgkin's disease or lipid histiocytosis (Gaucher's disease).

What is a Schilling hemogram? Illustrate by using the values for normal adults.

A Schilling hemogram consists of a leukocyte count and a classification of leukocyte types as they occur during a routine differential count. In normal adults the findings are: leukocyte count 5,000 to 8,000; basophils, 0 to 1 per cent; eosinophils, 2 to 4 per cent; myelocytes, 0 per cent; juvenile types, 0 to 1 per cent; stab cells, 3 to 5 per cent; segmenteds, 51 to 67 per cent; lymphocytes, 21 to 35 per cent; monocytes, 4 to 8 per cent.

Under what conditions are (1) a regenerative shift to the left and (2) a degenerative shift to the left encountered?

(1) Acute sepsis and appendicitis; (2) tuberculosis and typhoid fever.

Enumerate the diseases suggested by the findings of abnormal numbers of the following cell types in stained smears of peripheral blood: (1) myelocytes, (2) myeloblasts, (3) lymphoblasts, (4) Turk's irritation leukocytes, (5) plasma cells, (6) "basket cells."

(1) Myelogenous leukemia, pernicious anemia, anemia of malignancy; (2) acute and chronic myelogenous leukemia; (3) acute lymphatic leukemia; (4) primary and secondary anemia, leukemia, malaria, and leukocytosis of pneumonia; (5) multiple myeloma; (6) toxemia and leukemia.

Of what value are routine laboratory studies in predicting the tendency toward (1) hemorrhage and (2) thrombosis.

(1) Unfortunately, there are no tests that are sufficiently reliable to warrant their routine use to predict the tendency to bleed. The history of hemorrhagic phenomena is more reliable than all laboratory tests and must be taken seriously. In such cases, the most reliable tests in addition to the blood smear, white-cell count, and hematocrit are the thrombocyte count, the Ivy bleeding time, and the Quick one-stage "prothrombin time." (2) The routine laboratory studies are of little value in predicting postoperative thrombosis, for the condition of the blood vessel walls, spasm of blood vessels, and rate of flow are of greater importance than the hemic factors. A coagulation time of less than 5 minutes, a thrombocyte count greater than 1,000,000 per cu. mm., and a clot retraction beginning within 15 minutes are presumptive evidence of impending or existing thrombus formation.

Enumerate the factors which may cause defective blood clotting.

(1) Deficiency in number of thrombocytes leading to formation of a nonretractile clot, as in thrombopenic purpura, aplastic anemia, and lymphatic leukemia; (2) functional alteration in thrombocytes, leading to thromboplastin deficiency, as in hemophilia, aplastic anemia, and hemorrhagic disease of the newborn; (3) fibrinogen deficiency, as in cirrhosis and acute liver disease, associated with hemorrhage; (4) vitamin K deficiency, as in obstructive jaundice; (5) excessive antithrombin, as in hemorrhagic septicemia.

Aside from its value in the diagnosis of hematologic disorders, in what other diseases does examination of aspirated bone marrow assume diagnostic significance where examination of peripheral blood is inconclusive?

(1) Multiple myeloma and carcinomas metastasizing to bone, (2) malaria, (3) histoplasmosis, (4) miliary tuberculosis, (5) subacute bacterial endocarditis, (6) lupus erythematosus.

What is an L. E. cell and what is its significance?

An L. E. cell, or lupus erythematosus cell, is an abnormal destructive polymorphonuclear neutrophil containing a large, homogeneous, bluish-purple–staining inclusion body that appears to distend the cell and crowd the nucleus to one side. No chromatic pattern is seen in the inclusion body, a characteristic which distinguishes it from "tart cells." The L. E. cell occurs in the peripheral blood or bone marrow, or both, of a large proportion of patients with disseminated lupus erythematosus, and frequently clusters of L. E. cells surround a free mass of homogeneous material. These groupings are called L. E. "rosettes." While there is some difference of opinion regarding the complete significance of L. E. cells, experience has shown that the L. E. cell has considerable value in the diagnosis of lupus erythematosus and especially in differentiating it from rheumatoid arthritis and other collagen diseases with similar clinical manifestations. L. E. cells may be produced by penicillin, hydrolazine hydrochloride (Apresoline), and possibly other drugs.

Of what value is the determination of (1) coagulation time and (2) prothrombin time?

(1) In the diagnosis of hemorrhagic diseases, possible thromboses, and preoperatively where capillary oozing is suspected. (2) Preoperative management of patients with hepatic or gallbladder disease before or after administration of vitamin K; prior to, during, and after anticoagulant therapy.

Define and give an example of the occurrence of each of the following: (1) anisocytosis, (2) poikilocyte, (3) spherocyte, (4) polychromatophilia, (5) Howell-Jolly bodies, (6) target cells, (7) normoblast, (8) megaloblast, (9) Cabot's ring bodies, (10) sickle cell.

(1) Abnormal variation in erythrocyte size; pernicious anemia. (2) Variations in erythrocyte shape; pernicious anemia. (3) Almost spherical erythrocytes; congenital hemolytic icterus. (4) Abnormal erythrocyte affinity for basic stains; leukemia and pernicious anemia. (5) Nuclear particles seen in erythrocytes; pernicious anemia. (6) Erythrocytes characterized by a peripheral and central area of hemoglobin, between which lies an unstained area containing little hemoglobin; Cooley's erythroblastic anemia. (7) Nucleated erythrocyte; erythroblastosis fetalis. (8) Large erythroblast; pernicious anemia. (9) Ring-shaped or figure-of-eight shaped structures seen rarely in erythrocytes; may be a laboratory-created artifact; lymphatic leukemia. (10) Crescentic or fusiform-shaped erythrocytes; sickle-cell anemia.

Discuss glutathione (GSH) instability.

For years it has been known that certain drugs, in susceptible individuals, produced an acute anemia of the hemolytic type. This peculiar form of anemia occurred in approximately 10 per cent of Negro men who were given 30 mg. of primaquine a day. Further studies revealed that the susceptibility was hereditary, that it was sex-linked, and that Heinz bodies appeared in the erythrocytes after exposure to the drug. In susceptible individuals there was a reduction in the concentration of reduced glutathione when the red cells were exposed to offending toxic agents. The list of drugs that have a hemolytic effect on red cells includes antimalarial drugs, sulfanilamide, acetanalid, phenacetin, antipyrine, para-aminosalicylic acid, isoniazid, nitrofurantoin (Furadantin), tolbutamide (Orinase), and others.

Enumerate the salient hematologic findings in peripheral blood in (1) plumbism, (2) malaria, (3) congenital hemolytic anemia, (4) acute hemolytic anemia, (5) pernicious anemia, (6) aplastic anemia.

(1) Active erythropoiesis, basophilic stippling of red cells, mild oligocythemia. (2) Oligocythemia, moderate to marked granulocytosis with shift to the left; in mild cases, the anemia may be normocytic, in chronic cases, microcytic and hypochromic, with parasites in red cells. (3) Large numbers of spherocytes, increased erythrocyte fragility, marked poikilocytosis, reticulocytosis, marked to moderate leukocytosis with proportionate shift to the left. (4) A normochromic macrocytic anemia, marked leukocytosis, hemoglobinemia, and reticulocytosis; spherocytosis and increased capillary fragility are often seen; Coombs' test positive. (5) Mean corpuscular volume elevated, as is the mean corpuscular hemoglobin; the leukopenia involves principally the neutrophilic granulocytes, thereby producing a relative lymphocytosis; macrocytosis is the rule, anisocytosis is marked. (6) Marked oligocythemia with stained films showing characteristic sickle-shaped cells and evidence of phagocytosis of erythrocytes by monocytes;

microcytes and normoblasts are abundant; hemoglobin is elevated; moderate to severe leukocytosis is the rule.

What is meant by blood typing and how is it performed?

The determination of the blood group to which an individual belongs.

The following materials are required: (1) Supplies of serum from individuals known to belong to Groups A and B respectively. For convenience of identification, serum type A is faintly colored with methylene blue, and serum type B with fuchsin red. (2) A drop of blood from the patient and from each of the prospective donors. These drops of blood are diluted with salt solution.

A drop of each of the known sera is placed on the ends of a glass slide marked in such a way that there is no possibility of confusing the ends. To each end a drop of corpuscle suspension is added. If neither drop is agglutinated, the type is O; if serum B alone agglutinates the cells, the type is A; if serum A alone agglutinates the cells, the type is B; if both A and B agglutinate the cells, the type is AB.

An additional precautionary measure to avoid fatal accidents is the direct compatibility test. Dilutions of the cells of patient and donor, and a small amount of the serum of each are required. Be sure the specimens are *labeled correctly.*

1. Patient's cells .....Donor's serum
2. Patient's serum ....Donor's cells
3. Patient's serum ....Patient's cells (control)
4. Donor's serum ...Donor's cells (control)

If no agglutination takes place in any of the combinations, there is no incompatibility. If test 2 is positive, the donor must never be used. If the control tests are positive, it is of course a sign that there has been some mistake and the test must be repeated.

CYTOLOGY

List the cytological techniques that have improved the study of human chromosomes.

(1) The use of short-term tissue culture, including bone-marrow aspirates; (2) the use of colchicine to arrest mitosis before the formation of the spindle in the metaphase; (3) the use of hypotonic solutions to cause the cells to swell and to disperse the chromosomes; and, (4) the use of squash preparations rather than conventional tissue sections, so that the chromosomes can be examined more readily in one optical plane.

What is meant by exfoliative cytology? In what conditions may it be helpful? What is its over-all accuracy?

Examination of smears of material sloughed from the surface or lining of hollow viscera or cavities for the presence of malignant cells exfoliated from surface lesions (Papanicolaou method). Hyperchromatic nuclei, prominent nuclei, mitosis, and general clumping of cells varying with the viscus involved are significant, but not necessarily diagnostic. The accuracy of the method depends upon the experience of the observer and the source of the exfoliated cells. The greatest accuracy is reported from tumors of the female genital tract (90 per cent or over by some observers) and decreases in reliability through the respiratory tract, stomach, urinary tract, male genital tract, and lower bowel. Vaginal cytological examination is the simplest, most rapid, and least expensive method for estimating estrogen activity.

URINE ANALYSIS

What are the different steps in the routine examination of the urine?

Determine the appearance, pH reaction, and specific gravity. Test the urine for sugar with either Fehling's, Benedict's (qualitative), or Nylander's solutions, and Lenges' test for acetone. Centrifuge the urine. Examine the supernatant fluid for albumin with Exton's reagent, heat, or nitric acid.

Examine the sediment microscopically for the presence of casts, epithelial cells, blood cells, pus cells, and unorganized elements (uric acid crystals, etc.).

If albumin or sugar is present, a quantitative estimation should be made. Additional substances to be tested for are bilirubin, urobilinogen, bile pigment, indican, and chlorides. The diazo reaction is obtained in a number of infectious diseases, especially typhoid fever. Alkaloids, iodides, and phenols also give positive reactions.

In testing urine by heat in a case of suspected albuminuria, (1) what substance might be precipitated and so make the test deceptive? (2) How may these substances be differentiated from the precipitate of albumin?

(1) Earthy phosphates (calcium and magnesium phosphate), mucus. (2) By their solubility in acetic or nitric acid, albumin being insoluble.

Give two methods for the quantitative determination of albumin in urine.

Tsuchiya's Method: In a Shevky and Stafford tube add 25 cc. of Tsuchiya's reagent to 4 cc. of urine and mix. Let stand 10 minutes; centrifuge 10 minutes. Read the volume of precipitate and calculate the result by multiplying by a constant (previously obtained from a solution of known protein content).

Folin's Method: Add sulfosalicylic acid solution to urine. Compare the resultant turbid solution with prepared standard suspension of barium sulfate; read the turbidity in the nephelometer.

What glycoprotein may be present in normal urine and how is its presence detected?

Mucin. Dilute urine with about 3 volumes of water, strongly acidify with glacial acetic acid. Do not heat. Turbidity indicates a positive reaction. Albumin is not precipitated by this concentration of acid.

Give a test for proteosuria.

Acidify the urine with acetic acid and filter off any precipitate of nucleoprotein. Boil for several minutes. Filter while hot to remove albumin and globulin. Test the cooled filtrate by overlaying a saturated solution of trichloroacetic acid. A white ring at point of contact indicates proteoses; primary and secondary forms may be saturated by half and complete saturation with ammonium sulfate.

Give a test for Bence Jones proteins in the urine.

Heat the urine slowly in the water bath. Turbidity will occur at about 40°C. and precipitation at 60°C. Acidulate slightly with acetic acid and boil. The precipitate now partially or totally disappears. Allow to cool and, if Bence Jones proteins are present, the precipitate will *reappear.*

Describe the tests you would employ in testing urine for glycosuria.

Fehling's Test: Mix 1 cc. of Fehling's solution A & B with about 6 cc. of water and boil, then slowly add urine and boil after each addition; a yellow precipitate of cuprous hydroxide or a red precipitate of cuprous oxide is produced if glucose is present.

Nylander's Test: To about 10 cc. of urine add 1 cc. Nylander's reagent (bismuth subnitrate, 2 parts; Rochelle salt, 4 parts; and caustic soda, 8 per cent solution, 100 parts) and boil; in the presence of sugar the bismuth subnitrate is reduced to bismuthous oxide or metallic bismuth. The mixture assumes a grayish, dark brown, or black color, and, on standing, the precipitate together with the earthy phosphates settles to the bottom of the tube.

Benedict's Test: To 5 cc. of Benedict's reagent in a test tube, add 6 to 8 drops of urine (no more) and place the tube in boiling water for five minutes; then cool slowly. In the presence of glucose in the urine the entire solution will be filled with a precipitate that may be red, yellow, or green. Traces (less than 0.1 per cent) of glucose may cause the precipitate to form only on cooling.

Describe tests for determining acetonuria.

Ross Modification of Rottern Test: Place 1 gm. of reagent (1 gm. sodium nitroprusside and 100 gm. ammonium sulfate) in test tube and add 5 ml. filtered urine. Wait until powder dissolves and overlay with ammonium hydroxide. A red to purple color at line of contact indicates acetone.

Frommer's Test: To 10 ml. urine add 3 ml. 40 per cent sodium hydroxide. Add 10 drops of 10 per cent alcoholic solution of salicylaldehyde. Mix and heat upper portion to 70 for 5 to 10 minutes. Orange color, changing to deep red, appears in heated portion.

Give a test for diacetic (acetoacetic) acid in the urine.

A few cubic centimeters of urine are treated with a few drops of ferric chloride solution. The reddish phosphatic precipitate which forms is removed by filtration. The filtrate is treated with a few more drops of ferric chloride; in the presence of diacetic acid a red color develops that fades on standing or is rapidly discharged by boiling the solution.

What substances ingested are eliminated in the urine, which, with ferric chloride, yield a reaction similar to that of diacetic acid? How may they be distinguished from diacetic acid?

Salicylic acid, antipyrine, and other phenol products.

Differentiation: The red color produced by ferric chloride with diacetic acid is discharged upon the application of heat, but is not so discharged when produced by the other compounds mentioned. If the urine is boiled before treatment with ferric chloride, diacetic acid fails to produce a color; the other compounds yield the red color.

To what is the term "alkaptonuria" applied, and what is the origin of the substance which produces it?

To a urine containing homogentisic acid; this readily oxidizes on exposure to the air and sunlight, changing the color of the urine to a dark brown to black. It has the property of reducing Fehling's solution, yielding a black precipitate. Homogentisic acid is formed from tyrosine, which is a cleavage product of the protein molecule in intestinal digestion.

Give a test for alkaptonuria.

Urine rendered distinctly alkaline with sodium hydroxide and shaken becomes dark brown to black if homogentisic acid is present.

Give a practical method for the quantitative determination of chlorides in the urine.

Precipitate the chlorides in a known volume of urine with standard silver nitrate solution and nitric acid. Titrate with ammonium thiocyanate, using ferric alum as an indicator. Standardize the thiocyanate solution against the same silver nitrate solution.

Give a test for the detection of phosphates in the urine.

Render some urine distinctly acid by means of nitric acid, add some ammonium molybdate solution, and boil. A yellow precipitate of ammonium phosphomolybdate indicates the presence of phosphates.

Describe a test for (1) bilirubin, (2) urobilin, (3) hemoglobin, (4) hemosiderin, and (5) melanin in the urine. What interpretation should be placed upon positive findings in each instance?

(1) To 10 ml. urine in a test tube, add 5 ml. of a 10 per cent barium chloride solution. Mix and filter. To the insoluble

precipitate, add 1 to 2 drops Fouchet's reagent. A green or blue color indicates the presence of bilirubin. Evidence of liver damage and particularly hepatitis in its early stages. (2) To 10 cc. of filtered urine, clarified by treatment with barium chloride, add several drops of Lugol's iodine solution. Add 10 cc. saturated alcoholic solution of zinc acetate. Examine for green fluorescence when viewed in a bright light. Evidence of liver damage, biliary obstruction. (3) To 2 to 3 cc. of urine, add an equal volume of benzidine reagent and hydrogen peroxide. A blue color indicates the presence of hemoglobin. Evidence of extensive destruction of erythrocytes as a result of exogenous or endogenous causes. (4) Centrifuge 10 ml. of urine and pour off the clear supernatant fluid. To the sediment, add 10 cc. of a mixture consisting of equal parts of a 2 per cent potassium ferrocyanide solution and 1 per cent hydrochloric acid. Allow to stand 10 minutes, centrifuge and examine the sediment microscopically. Granules of hemosiderin appear blue, indicative of hemolytic anemia, hemochromatosis, and siderosis of the kidney. (5) To 10 cc. of urine, add an equal volume of bromide water. Formation of a yellow precipitate which blackens on standing is a positive reaction. Occurs in most cases of melanotic tumor.

Of what value is the determination of urinary 17-ketosteroids?

As an index of the combined activity of the adrenal cortex and gonads in males and an index of adrenal cortex activity alone in the female. Children under 6 years of age excrete less than 1 mg. per 24 hours. Adult females excrete 5 to 15 mg.; adult males 7 to 27 mg. per 24 hours. Diminished 17-ketosteroids are seen in cases of hypopituitarism, male hypogonadism, Addison's disease, and myxedema. Greater than normal amounts are excreted in adrenocortical carcinoma and hyperplasia of the suprarenal cortex.

Enumerate the different renal function tests, giving an example of each.

(1) Concentration tests: Fishberg and Lashmet and Newburgh. (2) Dye tests based on excretion of foreign substances: phenolsulfonphthalein. (3) Clearance tests based on the removal of nitrogenous constituents of the blood, including *p*-aminohippuric acid, mannitol, inulin, urea. (4) Blood nonprotein nitrogen determination: urea nitrogen retention.

What is the Sulkowitch test?

The Sulkowitch test is a practical semiquantitative method for estimating the concentration of calcium in the urine. It is useful as a screening test and as a guide to the proper dosage of oleovitamin D and calcium in the treatment of patients with hypoparathyroidism. Hypocalcemia is probably present if the patient's urine shows no precipitate or turbidity.

What casts are frequently found in albuminous urine and what do they denote?

Hyaline: Subacute and chronic nephritis, less often in the acute form; occur also in puerperal eclampsia, cancer, anemia, and, according to some, in normal urine.

Granular: Usually in acute glomerulonephritis, also in chronic nephrosis (large granular casts), and puerperal eclampsia.

Epithelial: Indicate an acute process; occur in acute nephrosis, particularly the form seen in scarlet fever, typhoid, pneumonia, and other infections.

Blood: Acute forms of nephritis, especially traumatic and toxic; do not indicate permanent structural change.

Waxy or Amyloid: Give the amyloid reaction; occur in chronic and occasionally in acute nephrosis; in phthisis, amyloid disease, and septic processes.

Urate Casts or Pseudocasts: Conglomerations of urates, not true casts; they are found in renal congestion, plethora, rheumatism, and tonsillitis.

EXAMINATION OF FECES

List the important points to be noted in the routine examination of feces.

The important points to be noted are:

Color: Clay or putty, yellow, brown, black, tarry, or combinations.

Consistency: Liquid, mushy, soft, formed, hard or scybalous.

Abnormal Constituents: Gross blood, mucus, pus, undigested food.

Reaction: Test a suspension with litmus or nitrazine paper.

Whenever indicated, a specimen should be sent to the laboratory for chemical and microscopic study.

How is occult blood detected in the feces?

The benzidine test and the orthotoluidine test are very sensitive; it is advisable to have the patient on a meat-free diet for at least 72 hours before either of these is done. Since many raw vegetables contain peroxidases that may produce a positive reaction, they too should be omitted. In doubtful cases, boiling a suspension of feces before performing the test will eliminate these peroxidases without interfering with the pseudoperoxidases of the erythrocytes. The guaiac test is less sensitive but, since no special preparation is required, it is more useful for screening purposes or as an office procedure.

Since small amounts of blood from hemorrhoids or other rectal lesions may be present on the surface of the stool, it is preferable to take material from the center of the specimen. If possible, a large amount is taken and a suspension prepared from this. After rectal examination, the fecal material on the glove can be used for these tests.

It is stated that when a person is on a meat-free diet, orthotoluidine will detect 1.0 ml. of ingested blood; benzidine will detect 3.5 ml., and guaiac 20.0 ml. Iron salts administered orally do not give a positive test with orthotoluidine or benzidine, and rarely interfere with the guaiac test.

Benzidine Test: Place 25 mg. (or several crystals) of reagent benzidine in a test tube or on a porcelain spot plate; add 0.5 ml. of glacial acetic acid and 0.5 ml. of 3 per cent hydrogen peroxide solution. Stir in a small portion of feces or add 2 ml. of a suspension of feces. A blue color, which appears within 30 seconds, shows that blood is present; the amount is roughly proportional to the intensity of the color.

Guaiac Test: Smear a small portion of feces on a piece of filter paper, or prepare a suspension and moisten the center of the paper with this. Add 2 drops of fresh alcoholic solution of guaiac (1.0 gm. of guaiac in 5.0 ml. of 95 per cent ethanol). Add 2 drops of glacial acetic acid, and 2 drops of "commercial" 3 per cent hydrogen peroxide solution. A blue color, which appears within 30 seconds, is a positive test; it can be graded according to the intensity of the color.

Give two tests for determining stercobilinogen.

Stercobilinogen (feces urobilinogen) is the principal end product of heme breakdown. The daily production is proportional to the mass of hemoglobin catabolized, and serves as a guide to the rate of blood destruction. In the differential diagnosis of hepatic disease, this test may be of value because of the fact that the obstruction due to a calculus is rarely as complete as that due to carcinoma of the head of the pancreas.

Qualitative Test: The Ehrlich reaction and the alcoholic zinc acetate test are applied directly to a portion of feces collected at random. These simple procedures will suffice for most purposes.

Quantitative Test: If biliary obstruction exists, collect all of the patient's feces for four days; this prolonged collection period greatly increases the accuracy of the test.

The normal output of stercobilinogen ranges from 40 to 300 mg. per 24 hours, or from 50 to 350 E.U. Values higher than this are believed to be due to abnormally increased blood destruction. In hemolytic anemia, with or without jaundice, the excretion may rise to 2,000 mg. daily. Complete obstruction of the biliary passages is characterized by values of 5 mg. or less; such low values are infrequently found except when the obstruction is due to a neoplasm. In rare instances hepatitis may cause complete suppression of bile secretion; usually this is transitory, but it has been known to persist for a number of weeks.

BIOCHEMISTRY

Define milliequivalents.

Although present-day students are taught to think of electrolytes in terms of milliequivalents rather than milligrams, older physicians occasionally find it difficult to understand or to readjust to the new concept. This may be less difficult if one remembers that an "equivalent" represents the amount of a given substance that can combine with, or can replace, an atom of hydrogen, and that a "milliequivalent" (mEq.) is the amount of the given substance that can combine with, or can replace, *one milligram* of hydrogen in 100 ml.

Since hydrogen is considered to have an atomic weight of 1, the weight of 1 mEq. of any substance (in milligrams) is equal to the atomic weight in the case of univalent ions, such as sodium, potassium, or chloride. Thus 23 mg. of sodium or 39 mg. of potassium can replace 1 mg. of hydrogen, or 35.5 mg. of chlorine can combine with 1 mg. of hydrogen; each represents 1 mEq.

For bivalent or polyvalent substances such as calcium, magnesium, or the sulfate radical, 1 mEq. is the atomic weight divided by the valence. Thus 10 mg. of calcium (20/2) or 12 mg. of magnesium (24/2) can replace 1 mg. of hydrogen, or 48 mg. of SO_4 (96/2) can combine with 1 mg. of hydrogen. Each of these represents 1 mEq.

Calculation of mEq./Liter from mg./100 ml.

	CONVERSION FACTOR *	× NORMAL RANGE mg./100 ml.	= NORMAL RANGE mEq./liter
Na	0.435	308-331	134-144
K	0.257	13.6-20.7	3.5-5.3
Ca	0.500	9-11.4	4.5-5.7
Mg	0.833	1.36-2.5	1.2-2.2
HCO_3			
(CO_2 vol.%)	0.455	54-68	24-31
Cl (as NaCl)	0.171	573-632	98-108
(as Cl)	0.286	343-378	98-108
PO_4	0.58	4.65-7.6	2.7-4.4
SO_4	0.625	1.6-2.4	1.0-1.5

* To convert mEq. per liter to mg. per 100 ml., *divide* by the factor given above.

The table gives the average values for the more common ions, both in milligrams per 100 ml. and in mEq. per liter. The conversion factor for changing one to the other is also indicated for each substance. The conversion factors can be calculated from the fraction $\frac{10}{\text{at. wt.}}$, i.e., $\frac{10}{23} = 0.435$ the conversion factor for sodium.

Give the normal amounts in the blood of urea nitrogen, nonprotein nitrogen, creatinine, sugar, uric acid, plasma cholesterol, plasma CO_2 capacity, plasma protein (total), plasma albumin, plasma globulin, serum phosphorus (adult), serum phosphorus (child), serum bilirubin (van den Bergh).

	NORMAL
Urea nitrogen	10-22 mg. per 100 cc.
Nonprotein nitrogen	25-30 mg. per 100 cc.
Creatinine	1-2 mg. per 100 cc.
Sugar	80-120 mg. per 100 cc.
Uric acid	2-4 mg. per 100 cc.
Plasma cholesterol	110-300 mg. per 100 cc.
Plasma CO_2 capacity	50-60 vol. per cent per 100 cc.
Serum protein (total)	6-8 gm. per 100 cc.
Serum albumin	4.0-5.5 gm. per 100 cc.
Serum globulin	1.3-3.4 gm. per 100 cc.
Serum phosphorus (adult)	3-4.5 mg. per 100 cc.
Serum phosphorus (child)	5-6 mg. per 100 cc.
Serum bilirubin (van den Bergh)	0.2-1 mg. per 100 cc.

Give a general method for estimating the quantity of glucose in the blood.

The proteins are precipitated by any of the recognized methods. One method is to take 2 cc. of blood, add 14 cc. of distilled water, add 2 cc. of 10 per cent sodium tungstate solution and 2 cc. of two-thirds normal sulfuric acid. Shake and filter. To determine the glucose in the blood, take 2 cc. of the protein-free filtrate containing 0.2 cc. of blood and transfer to a Folin blood sugar tube. To a second tube add 2 cc. of a standard sugar solution containing 0.2 mg. of dextrose. To each tube add 2 cc. of alkaline copper tartrate solution and mix. Place the tubes in boiling water for six minutes and then cool. To each tube 2 cc. of molybdate phosphate solution is added, and after a few minutes distilled water is added up to the 25 cc. mark. The color of the mixture is then compared in a colorimeter with the standard. If the unknown is set at 20, the blood sugar, in milligrams per cent, is the reading of the standard multiplied by 5.

What is the significance of the blood sugar tolerance test?

Normally, the blood sugar rises gradually from the fasting level to 150 to 175 mg. of dextrose per 100 cc. at the end of the first hour, and returns to the original level by the end of the third hour. No sugar is found in the urine. *Diminished* tolerance is noted by a higher peak and a slower return and by the appearance of sugar in the urine. This is typical of diabetes and also of liver disease, endocrine disorders and nutritional deficiencies. *Increased* sugar tolerance is indicated by a low initial blood sugar (hypoglycemia), a slight rise, and rapid return to the original level. This is seen in hyperinsulinism, dysinsulinism, myxedema, hypothyroidism, Addison's disease, pituitary disorders, and pancreatic tumors.

In what conditions is the blood urea nitrogen elevated?

Elevation of the blood urea nitrogen is indicative of kidney damage and is seen in chronic or acute glomerulonephritis and in chronic pyelonephritis or arteriolar nephrosclerosis. It is also seen in obstructive uropathies caused by stone, hypertrophy of the prostate, and kinked ureter. The blood urea nitrogen is also elevated in dehydrated states, hemolytic anemias, intestinal obstruction, diabetic coma, poisoning with mercury, and in traumatic shock.

In what conditions is the blood uric acid increased?

In early nephritis uric acid is increased earlier than the urea and nonprotein nitrogen. After a diet rich in purine bodies there is also an elevation. In gout, lead poisoning, leukemia, and in any condition in which there is destruction of body cells, a high uric acid content is found.

What is the significance of the blood cholesterol?

Low concentrations of serum cholesterol are found in hyperthyroidism, in starvation or prolonged malnutrition, in steatorrhea, in advanced renal disease, in the late stages of chronic hepatic fibrosis, during severe hepatic necrosis, in febrile infectious diseases, in anemias of various etiologies, and in the terminal stages of many diseases.

Elevated serum cholesterol concentrations are found in poorly controlled diabetes mellitus, in the nephrotic syndrome, in biliary-tract obstruction, in hypothyroidism and myxedema, in Christian's syndrome (Hand-Schüller-Christian), after acute hemorrhage, and during the later months of pregnancy. Many patients with arteriosclerosis and coronary-artery disease have an elevated serum cholesterol; this may be on a hereditary basis. The same is true in the condition known as idiopathic familial lipemia. It should be noted that values as high as 350 mg. per 100 ml. may be found in normal individuals. The serum cholesterol rises slowly with advancing age.

Discuss the calcium-phosphorus ratio in the blood.

The normal calcium content of the blood serum in adults is 9 to 11 mg. in 100 cc.; in children, 10 to 12 mg. Normal inorganic phosphorus varies from 3 to 4.5 mg. per 100 cc. in the adult; 5 to 6 mg. in children.

In infantile tetany very low serum calcium values are encountered (3.5 to 7 mg.). This is also the case in tetany following parathyroid removal. The phosphorus is correspondingly increased.

The blood calcium is decreased in osteoporosis. High serum calcium is the rule after parathyroid extract administration and in the presence of a tumor of the parathyroid; low phosphorus is associated. Vitamin D stimulates parathyroid activity, causing an increase of blood calcium.

With increased blood calcium there is increased excretion of calcium in the urine as calcium phosphate, causing a decrease or loss of the blood phosphates.

In rickets a low inorganic blood phosphorus is usually found, especially in severe cases. High phosphorus is the rule in diseases of the kidney with urinary suppression.

In what conditions is an elevation of the basal metabolic rate found? In what conditions is it low?

Increased in hyperthyroidism, hyperpituitarism, leukemia, severe anemias, some malignant conditions, Hodgkin's disease, hypertension, asthma, congestive heart failure, pheochromocytoma, fever (10 per cent increase for each degree Fahrenheit rise of body temperature), severe acidosis, convalescence from wasting diseases, and rapid growth.

Decreased in hypothyroidism, after thyroidectomy, in myxedema, cretinism, thyroid obesity, hypopituitarism, hypophyseal obesity, hypoadrenalism, Addison's disease, Simmonds' disease, starvation, liver disease, endocrine disorders, and nutritional deficiencies.

What is the van den Bergh test? How is it performed? What are its interpretations?

It is a test to measure the amount of bilirubin in the blood and its nature.

Technique: DIRECT REACTION: Place 1 ml. serum in a graduated centrifuge tube. Slant to an almost horizontal position and allow 0.5 ml. of Ehrlich's diazo reagent to run down the wall of the tube. A *positive* reaction is the prompt appearance of a reddish color at the junction, which becomes maximal in less than 60 seconds. After completion of the direct test, if positive, shake the tube and add 3 ml. 95 per cent ethanol (containing a trace of ether). With the appearance of a pink or ruby color, add 1 ml. saturated ammonium sulfate solution, shake gently and centrifuge 5 to 10 minutes. Determine the volume of only the uppermost ruby red layer from the graduations on tube.

Interpretation: A positive direct reaction indicates the presence of obstructive jaundice. A delayed direct reaction or an elevated indirect reaction indicates hemolytic jaundice or liver dysfunction. A serum bilirubin of 1.2 to 2.5 mg. per 100 cc. indicates latent jaundice. Clinical jaundice is present if the reading is higher than 2.5 mg. A diphasic reaction indicates parenchymatous liver disease with intrahepatic obstruction.

What is the Friedmann test?

A test upon the urine of women for pregnancy, hydatid mole, or choriocarcinoma; or the urine of men for the presence of abnormal amounts of gonadotropin, as in the presence of a testicular choriocarcinoma.

Describe Levinson's test on cerebrospinal fluid and discuss its significance.

This test is supposedly specific as a diagnostic tool for tuberculous meningitis. In each of two flat-bottomed test tubes graduated to 2 cc. place 1 cc. of spinal fluid. To one test tube add 1 cc. of 1 per cent aqueous solution of mercuric chloride, and to the other test tube add 1 cc. of 3 per cent aqueous sulfosalicylic acid. Stopper, shake, and let stand for 24 hours. Read the height of the precipitate in each tube and determine the ratio. In normal CSF, the volume of precipitates in both tubes is very slight. In suppurative meningitides, the sulfosalicylic precipitate is large, often three times that seen in the mercuric chloride tube. In tuberculous meningitis, the opposite occurs, the mercuric chloride precipitate being about three times larger than the sulfosalicylic acid one.

Describe the micro method (Shock and Hastings) for acid-base balance studies.

Cutaneous blood, equivalent to arterial blood in its properties, is collected in samples of 0.5 to 1.0 ml.; aliquots of 0.1 ml. are taken up in special pipettes and analyzed for packed red cell volume, colorimetric pH and CO_2 content. From these data can be calculated other factors important in the acid-base balance, such as arterial (or alveolar) CO_2 pressure (pCO_2) and whole blood buffer base $(BB^+)b$. The pCO_2 indicates the respiratory component of the disturbance, if any, and the $(BB^+)b$ the metabolic component. The $(BB^+)b$ is a better index of excess or deficit of fixed acids or base in the blood than is the serum bicarbonate or CO_2 concentration, because it includes other buffers (e.g., hemoglobin) as well as the bicarbonate. The method is useful in the more precise diagnosis of acid-base disturbances and in the control of therapy, and is especially adapted to pediatric work because of the small amount of blood required.

List the liver function tests which are indicated as initial studies (*a*) in detection of liver damage in the absence of jaundice; (*b*) in detection of residual liver damage in chronic hepatitis, Laennec's cirrhosis; (*c*) following the course of the jaundiced patient suffering from parenchymatous disease; (*d*) in differentiation of jaundice due to biliary disease from that due to parenchymatous disease; (*e*) in differentiation of extrahepatic biliary obstruction due to calculus from that due to neoplasm; (*f*) in detection of hemolytic disease.

(*a*) BSP, direct and total bilirubin, cephalin flocculation, thymol turbidity and flocculation, zinc turbidity, and urine urobilinogen; (*b*) BSP, direct and total bilirubin, and the flocculation group; (*c*) direct and total bilirubin, flocculation group, serum albumin and globulin, prothrombin, total and esterified cholesterol; (*d*) serum alkaline phosphatase; (*e*) feces urobilinogen; (*f*) direct and total bilirubin and feces urobilinogen.

Give the standard values for the following chemical constituents of blood: (*a*) bromsulfalein (45 minute test; 5 mg./kg.); (*b*) cholinesterase, serum; (*c*) phosphatase, alkaline, serum, adult; (*d*) phosphatase, alkaline, serum, infant.

(*a*) 0-6.9 per cent retention; (*b*) 0.55-1.15 Michel units; (*c*) 2.2-8.5 Shenowara units; (*d*) 5-16 Shenowara units.

Which laboratory tests are useful in determining when (*a*) liver parenchyma is involved; (*b*) the biliary tract is involved; and, (*c*) both are involved?

(*a*) Cephalin and thymol flocculation tests; (*b*) alkaline phosphatase and serum cholesterol; (*c*) serum bilirubin.

Normal Values, Cutaneous Blood, Adults

RED-CELL VOLUME, %	PH	WHOLE BLOOD CO_2, MM./L.	CALCULATED CO_2 PRESSURE, MM. HG	CALCULATED BLOOD BUFFER BASE, MEQ.
46	7.40 + 0.05	22 ± 2	40 ± 5	49 ± 3

Indicate the liver function test findings usually seen in: (*a*) viral hepatitis, no jaundice; (*b*) cholangiolitic jaundice; (*c*) complete extrahepatic obstruction; (*d*) biliary cirrhosis.

(*a*) Bilirubin may be present in urine and slightly elevated in serum; urobilinogen present in urine; BSP abnormal, flocculation tests abnormal; tests of biliary-tract involvement are normal. (*b*) Bilirubin increased in urine and serum, A/G usually normal; elevated phosphatase and lipid; good response to vitamin K. (*c*) Bilirubin extremely elevated; very low fecal urobilinogen, elevated phosphatase and lipid; good response to vitamin K. (*d*) Elevated bilirubin, BSP increased, A/G abnormal; thymol turbidity increased, elevated phosphatase and lipid, especially phospholipid.

What enzyme studies are indicated in a case of acute pancreatitis?

Serum lipase and serum amylase. In normal adults these constituents are present in blood in the following concentrations: serum amylase (males), 49-161 units; serum amylase (females), 28-137 units; serum lipase, 0.05-1.0 units. In acute pancreatitis, both amylase and lipase rise sharply; however, within two to three days the amylase level may return to normal.

List the different types of hemoglobin and their occurrence.

Type A: Normal adult.

Type F: Fetus, newborn; thalassemia, sickle-cell disease.

Type S: Sickle-cell anemia and sickle-cell trait; in combination with Hb-C and Hb-D and in thalassemia.

Type C: Hb-C disease, Hb-C trait; sickle-cell Hb-C disease.

Type D: Hb-D trait, Hb-D-Hb-S disease.

Type E: With F in atypical anemia.

What is the significance of the determination of plasma "protein-bound iodine" (PBI) and what factors influence the values obtained?

The determination of PBI represents one of the most direct approaches to the evaluation of the state of thyroid function. Interpretation of abnormalities in PBI are based on the premise that elevated or diminished PBI values reflect hyper- or hyposecretion of thyroid hormone. In addition, the determination may be useful in indicating the nonthyroid basis for basal metabolic rate elevations due to other causes and in suggesting the presence of hyperthyroidism at basal metabolic rate levels within the normal range. Important sources of error that influence PBI values are: (1) large amounts of nonhormonal iodine, (2) administration of radiopaque iodine compounds, (3) administration of mercurial diuretics, (4) medication with antithyroid agents, (5) administration of radioactive iodine.

Of what value are radioiodine studies? Explain what is meant by "conversion ratio of I^{131}."

Radioiodine studies measure two functions of the thyroid gland: (1) its capacity for accumulating iodine, and (2) its capacity for retaining organically bound iodine. These functions are evaluated by: (1) measuring, by means of scintillation counters, the thyroid uptake of I^{131} after oral administration of 5 to 50 μc. of I^{131} as potassium or sodium iodide, and (2) estimating the urinary excretion of I^{131} during a 24- to 48-hour period following the test dose. Some investigators feel that urinary excretion of I^{131} during a 12- to 24-hour interval is more valuable diagnostically in hyperthyroidism, while an interval of 72 hours is desirable in hypothyroidism.

The conversion ratio of I^{131} expressed as

$$\frac{\text{plasma protein-bound } I^{131}}{\text{total plasma } I^{131}} \times 100$$

is an index of thyroid hormone release into the peripheral circulation. The ratio is obtained by analysis of plasma and protein precipitate for I^{131} 24 hours after oral administration of 100 μc. I^{131}. In euthyroid subjects, the conversion ratio is 15 to 40 per cent; in hyperthyroidism, it is increased to 50 to 100 per cent, while in hypothyroidism, it is decreased to 0 to 5 per cent.

What is the principal clinical value of the determination of basal metabolic rate?

The value of the determination of basal metabolic rate in clinical practice lies in the exclusion of the thyroid gland as the cause of the patient's symptoms. About 95 per cent of individuals without thyroid disease have a basal metabolic rate lying in the range ±15.

Discuss glutamic oxalacetic and glutamic pyruvic transamination.

Transamination is a reversible enzymatic reaction in which an alpha-amino nitrogen of an amino acid is transferred to an alpha-keto acid, with the formation of a new amino acid and a new alpha-keto acid. Glutamic oxalacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) are such enzymes. While GOT has been shown to be present in all human and animal sera tested, markedly elevated concentrations have been shown to occur in patients during episodes of acute myocardial infarction, in patients suffering with parenchymal liver disease, in rheumatic fever with myocarditis, infectious mononucleosis and other disorders accompanied by some cardiac, hepatic, or muscle necrosis. Serum GPT is a more sensitive indicator of acute liver-cell injury than S-GOT and rises less than the latter in myocardial infarction. Thus S-GPT is of value in differentiating possible myocardial infarction and liver disease.

Discuss the possible mechanisms of causation of hypercalcemia associated with malignant disease.

Hypercalcemia, as one of the manifestations of malignant disease, has become a well-recognized phenomenon. Three possibilities have been postulated as to its mechanism: (1) The hypercalcemia may be secondary to bone metastases with breakdown of the bone matrix and subsequent release of more calcium into the circulation than can be cleared by the kidneys. However, many cases of malignant disease with hypercalcemia have been observed without bone destruction. (2) the tumors might produce a substance like vitamin D causing increased calcium absorption from the gastrointestinal tract similar to the defect noted in Boeck's sarcoid. (3) The tumor produces a substance with properties like parathormone, which is responsible for the hypercalcemia.

State whether the serum calcium, serum phosphorus, and serum alkaline phosphatase is increased, decreased, or remains normal in the following instances: (*a*) primary hyperparathyroidism, (*b*) osteomalacia, (*c*) "renal rickets," (*d*) acute osteoporosis, (*e*) osteomyelitis.

	CALCIUM	PHOSPHORUS	ALKALINE PHOSPHATASE
(*a*)	Normal	Decreased	Increased
(*b*)	Normal or decreased	Decreased	Increased
(*c*)	Decreased	Increased	Normal or slightly increased
(*d*)	Normal or increased	Normal or increased	Normal
(*e*)	Normal	Normal	Normal

What is the significance of an elevated serum acid phosphatase?

(1) Corroborates the diagnosis of metastatic prostatic cancer suggested by other methods of investigation. (2) Provides evidence of metastasis before this is otherwise demonstrable. (3) Indicates the prostatic origin of metastatic lesions when the primary tumor is undetectable clinically. (4) Aids the selection of cases suitable for castration or estrogen therapy.

What is the significance of an elevated serum alkaline phosphatase?

Serum alkaline phosphatase is a reflection of the activity of osteoblasts in diseases of bone. Elevations of this factor indicate: (1) inadequate mineralization or (2) injury, with (3) attempts at repair, which implies (4) adequate bone matrix.

Describe a test for adrenocortical insufficiency and more specifically for Addison's disease which is based upon responses observed following administration of ACTH. Discuss the limitations and interpretations of the test findings.

It has been demonstrated that certain profound effects occur in man after the injection of ACTH. In normal subjects and in patients with no adrenal insufficiency, certain of these effects occur in the blood and become manifest as a very marked drop in the number of circulating eosinophils, a less profound and less consistent fall in lymphocytes and an inconstant (nonspecific) rise in neutrophils. This ability to develop eosinopenia in the peripheral circulation after administration of a specified dose of ACTH forms the basis of a screening test widely employed for demonstration of normal function of adrenal cortex.

In general, the test consists of a determination of the number of eosinophils in the peripheral blood before and after intramuscular injection of a specified dose of ACTH. There exist a number of modifications of this basic procedure, among which the most useful are:

(*1*) *Four-Hour ACTH Test:* Since rather wide fluctuations in eosinophils occur during the morning hours, the test is conducted in the afternoon. Peripheral blood is drawn by venipuncture, after which 25 mg. ACTH is injected intramuscularly. A second specimen of blood is drawn 4 hours later. The number of eosinophils per cubic millimeter of each of the blood specimens is determined.

In normal individuals (eosinophil counts before ACTH = 150 to 300 per cu. mm.) eosinophils decrease 50 per cent or more 4 hours after injection of ACTH. No decrease or a decrease of less than 50 per cent suggests adrenocortical insufficiency, but this is not reliable diagnostically. However, normal response is occasionally seen in subjects with Addison's disease and false positives (inadequate response) in hypopituitarism.

(*2*) *48-Hour ACTH Test:* In certain situations, e.g., adrenal insufficiency secondary to anterior pituitary failure, eosinopenia may not develop because the atrophic adrenal cortex is insufficiently stimulated by a single ACTH injection. In these instances, the 48-hour test is apt to be more reliable. Blood for eosinophile count is drawn as in the four-hour test. Ten milligrams of ACTH is given intramuscularly every 6 hours over a 48-hour period and a second blood for eosinophile count drawn 4 hours after the last injection. Patients with Addison's disease fail to show a significant increase in eosinophils of 50 per cent or more. An adrenal cortex atrophied due to hypopituitarism will usually be stimulated to give a normal response. If desired, additional valuable information can be obtained from this test by a study of 17-ketosteroids and/or corticoids in 24-hour urine samples taken before and during the second day of the test. Normal subjects may show increases of 100 per cent or more of these steroids. In the addisonian patient, neither corticoids nor 17-ketosteroids are increased, whereas in hypopituitarism there is usually an appreciable rise from the low levels present before stimulation.

(*3*) *Intravenous ACTH Test:* Collect a 24-hour urine specimen for 17-ketosteroids and corticoids. Infuse 25 mg. ACTH in 500 ml. saline or glucose intravenously over an 8-hour period. Collect a second 24-hour urine specimen, starting at time of infusion. Collect peripheral blood specimens for eosinophile counts at 0, 6, and 10 hours after the start of the infusion. A normal response includes: (*a*) decrease in eosinophils of at least 85 per cent at 10 hours and (*b*) increase of 10 to 15 mg. in urinary 17-ketosteroids and corticoids.

What is meant by the Gibbs-Donnan effect? What is its physiologic significance?

The Gibbs-Donnan effect attempts to explain the nature of the equilibrium that is established between two solutions separated by a semipermeable membrane. Quantitative ionic relations existing at equilibrium may be stated as follows: (1) The concentration of diffusible cation is higher and that of diffusible anion is lower on the side of the membrane containing a nondiffusible anion in solution. (2) At equilibrium and under conditions of constant solvent volume, the sum of the concentrations of diffusible ions in the solution containing nondiffusible ion exceeds the sum of the concentrations of the same ions in the other solution. The former solution will therefore have the higher osmotic pressure.

The Gibbs-Donnan effect finds particular application in exchanges of Cl^- and HCO_3^- between blood plasma and erythrocyte and in water and ion exchanges between blood plasma and interstitial fluid.

Discuss the value, if any, of cerebrospinal fluid glucose concentration in the differential diagnosis of acute epidemic encephalitis and tuberculous meningitis.

In view of the varied symptomatology that characterizes acute epidemic encephalitis and the fact that this disease clinically simulates tuberculous meningitis, determination of cerebrospinal fluid glucose concentration very frequently aids in their differential diagnoses. Hyperglycorrhachia (increase in glucose content of spinal fluid) is the most frequent finding in acute epidemic encephalitis, whereas hypoglycorrhachia is an invariable feature of the fluid of tuberculous meningitis. Rarely is sugar entirely absent in tuberculous meningitis, as is frequently the case in the suppurative meningitides.

What is the purpose of the insulin tolerance test?

To determine the sensitivity of the organism to insulin and its responsiveness to insulin-induced hypoglycemia. Under normal conditions, the blood sugar falls to about 50 per cent of the fasting level 20 to 30 minutes after intravenous injection of 0.1 unit of insulin per kg. of body weight. It then rises rapidly, reaching the preinjection level in 90 to 120 minutes. The duration of hypoglycemia is of greater importance than its degree.

List the factors which may influence the basal metabolic rate.

The following factors may influence the basal metabolic rate: Barometric pressure; age–rate declines with advancing years; sex–lower in females than in males; menstruation–slight premenstrual rise; pregnancy–rise during the last trimester as a result of fetal metabolism; diet–lower in vegetarians than in those who eat meat; habits–higher in those engaged in work requiring muscular effort: climate; race. The first three factors are taken into consideration in calculating the basal metabolic rate from the known oxygen consumption. In children and adolescents who show excessive deviation from the normal range of height or weight, calculation of the basal metabolic rate may be erroneous because of the unreliability of the normal standards.

Outline the laboratory diagnosis of thyroid dysfunction.

Elsewhere are discussed the various laboratory procedures most commonly employed in the diagnosis of this disease. It is extremely difficult statistically to compare the accuracy of these several tests, since there are no controlled studies utilizing all of them concurrently. Furthermore, no one laboratory procedure is infallible and each, because of inherent inaccuracies, must be interpreted individually in the light of all clinical data. However, a general scheme can be arranged that would indicate the relative importance (i.e., percentage of accuracy) of these procedures in appraising thyroid function in an unselected population: cholesterol (20 to 50 per cent), BMR (50 to 70 per cent), PBI (70 to 85 per cent), and I^{131} uptake (80 to 90 per cent).

What are the different steps in the routine examination of the gastric contents?

(1) Test for basal gastric secretion without artificial stimulus: Aspirate stomach contents at 10-minute intervals for a period of 1 hour. (2) Histamine test of gastric function: as for the basal gastric secretion test, except that the patient receives a subcutaneous injection of histamine in a dosage of 0.01 mg. per kg. body weight 10 minutes prior to the beginning of aspirating the stomach contents. (3) Physical examination: quantity, appearance, and odor. (4) Chemical examination: total and free acidity, occult blood.

Define "tubeless gastric analysis."

This procedure demonstrates gastric HCl secretion without intubation of the stomach. It is based on the fact that when a quininium cation exchange resin mixes with free HCl it will release quinine in exchange for the H ion of the acid. The quinine is absorbed in the intestine and is excreted in the urine, where it can be determined quantitatively (histamine stimulation of gastric secretion is also employed). This procedure is useful as a screening test for achlorhydria: a positive quinine response eliminates the need for further study, but a negative response is not absolute proof of achlorhydria.

MICROBIOLOGY

Mention four fundamental divisions of microorganisms.

Bacteria, yeasts, molds, and viruses.

Define bacteria. State (a) methods for recognition and cultivation, (b) the different ways bacteria enter the body to produce disease.

(*a*) Bacteria are microscopic unicellular organisms, devoid of chlorophyll, and predominantly multiplying by fission. They are recognized by their shape, size, motility, grouping, behavior in different culture media, staining reactions, immunological reactions, and relative pathogenicity. The chief culture media are mixtures of simple inorganic compounds and complex organic materials, such as milk, blood serum, bouillon, gelatin, agar, potato. (*b*) Bacteria enter the body through the abraded skin or mucous membranes, or through the respiratory and alimentary tracts.

Discuss the classification of bacteria.

Bacteria do not belong strictly either to the animal or to the vegetable kingdom. While yeasts and molds are closely related to the plants, protozoa belong properly in the animal kingdom. For convenience, bacteria are classified with the fungi or colorless (nonchlorophyll-bearing) plants. Classification is based primarily on form (morphology), motility or nonmotility, the presence or absence of flagella and their situation, and spore formation. Other criteria are: cultural characteristics, biochemical reactions and pathogenic properties, staining, behavior on different media, fermentation, reaction to specific immune sera (agglutination, complement fixation). Morphology alone cannot be relied upon.

Give a broad classification of bacteria, based on morphologic differences, and name an example of each.

Cocci: *Streptococcus pyogenes;* bacilli: *Bacillus anthracis;* spirilla: *Treponema pallidum.*

(1) Define the following terms: (a) coccus, (b) bacillus, (c) spirillum, (d) strict anaerobe, (e) facultative anaerobe. (2) Name one anaerobic organism.

(1) (*a*) A spherical bacterium, (*b*) a rod-shaped bacterium, (*c*) a spiral or corkscrew-shaped bacterium, (*d*) a bacterium that grows only in the absence of atmospheric oxygen, (*e*) one that grows best in the presence of air, but will grow also in its absence. (2) *Clostridium tetani.*

(*a*) Name the pathogenic cocci. (*b*) Give the morphology and (c) method of staining of each. (*d*) Name the varieties usually found in furunculosis, tonsillitis, and purulent salpingitis.

(*a*) *Staphylococcus aureus* and *epidermidis; Gaffkya tetragena; Streptococcus pyogenes* and *faecalis; Neisseria gonorrhoeae* and *meningitidis;* and *Diplococcus pneumoniae.*

(*b*) Staphylococci occur singly, in pairs, in tetrads, and in irregular masses or clusters, like bunches of grapes; streptococci are in chains; gonococci and meningococci (*Neisseria*) are shaped like coffee beans; diplococci are in pairs, of which the pneumococcus is the type.

(*c*) They are all stained with Gram's stain.

(*d*) *Staphylococcus aureus;* micrococcus, *streptococcus,* and pneumococcus; gonococcus.

Define the following: (*a*) pathogenic, (*b*) saprophytic, (c) leukocytes, (*d*) phagocytes, (e) opsonins.

(*a*) Capable of producing disease. (*b*) Bacteria that feed on dead organic matter and usually not pathogenic. (*c*) The white or colorless corpuscles of the blood. (*d*) Leukocytes (polymorphonuclear) and endothelial cells capable of taking up and devouring inert particles and dead and living bacteria. (*e*) Substances contained in the blood serum that act on bacterial cells in such a way that the leukocytes are enabled to take them up and digest them by the process of phagocytosis.

Discuss the question of bacteriophage.

The true nature of bacteriophage is still in doubt. According to d'Herelle it is a living microorganism, ultramicroscopic, filterable, and a parasite of bacteria. He proposed the term *lytic filtrate* or *protobe.* According to another view bacteriophage is an *enzyme;* a third theory holds that the phenomenon is a form of *autolysis of bacteria.* The substance, whatever its nature, is present in animal tissue, especially the intestinal tract. It was originally obtained by adding 2 or 3 drops of a dysentery stool to 20 cc. of broth and filtering through a Chamberland candle. It is also obtainable from intestinal mucous membrane. It acts on young, growing cultures only and can be carried on from generation to generation but is not transmitted by dead bacteria. An alkaline medium and aerobic conditions are required. It resists higher temperatures than bacteria—up to 65°C.—but is destroyed by exposure to 75°C. for thirty minutes. It is resistant to acetone, alcohol, chloroform, and glycerin. Colonies to which bacteriophage has been added become "glassy" on standing, forming "water of condensation."

Bacteriophage has been used clinically in the treatment of infections—typhoid fever, dysentery, cholera, and plague—but has not proved itself. However, recent studies have indicated the value of phage-typing for bacterial identification or "epidemiological fingerprinting" of certain microorganisms, particularly *Staphylococcus aureus.* The phage-typing of staphylococci has provided unequivocal evidence that hospital cross-infection with staphylococci is widespread and is largely responsible for the many antibiotic-resistant strains among hospital patients, especially in maternity and surgical wards.

On what two factors does the virulence of bacteria depend?

(*1*) *Invasiveness:* The invasiveness of bacteria depends on the ability of the organism to metabolize human substance and to escape the action of leukocytes; also to grow rapidly in spite of antibodies. In this way, the bacteria gain admission to the blood stream, giving rise to a bacteremia.

(*2*) *Toxigenicity:* Some organisms attain their virulence by secreting exotoxins that are absorbed by the blood and later by other tissues, such as the nerves (tetanus bacillus).

Discuss two types of toxins, (*a*) endotoxins, (*b*) exotoxins.

(*a*) *Endotoxins:* Poisonous decomposition products associated with disintegration of the bacterial body.

(*b*) *Exotoxins:* Soluble metabolic products secreted and excreted by the organism.

What is meant by bacterial dissociation?

Some bacteria in pure culture produce multiple types of growths that are different from the original strain in essential properties.

What is meant by a carrier?

This refers to a person who has recovered from a disease but continues to harbor the infecting organisms, thereby being able to transmit the disease to others. Typhoid fever (gallbladder) and meningococcus infections (nasopharynx) are diseases in which the carrier state is seen.

Describe a practical method of staining for *Treponema pallidum* (*Spirochaeta pallida*).

A drop of "tissue-juice" as free from blood as possible is obtained by lightly scraping the lesion and is smeared on a slide to form a thin film. It is dried by passing through a flame, and is fixed by immersion in alcohol and ether for five minutes. The stain is then applied for fifteen to twenty minutes, and the slide is washed in water and allowed to dry. *Treponema pallidum* stains light red with Giemsa's stain. Examination of dry, stained films is not so satisfactory as examination of a wet specimen.

A convenient and very reliable method of demonstrating *Treponema pallidum* in the living state is by means of the *darkfield illuminator* or condenser, which can be attached to any microscope.

Name the important pathogenic anaerobes.

Clostridium perfringens, Cl. novyi, Cl. septicum, Cl. tetani, Cl. histolyticum, Cl. botulinum.

What are pyogenic bacteria?

Bacteria that produce pus.

What is a diplococcus? Give the names of the important pathogenic diplococci.

Diplococci are cocci or spherical bacteria occurring in pairs. (1) *Diplococcus pneumoniae,* or pneumococcus; (2) *Neisseria gonorrhoeae,* or gonococcus; (3) *N. meningitidis,* meningococcus.

Define the following terms: chemotherapeutic, germicide, antiseptic, asepsis, sterile, disinfectant, antibiotic.

A *chemotherapeutic* is a chemical substance that is sufficiently nontoxic to the host to permit its use in the treatment of infections within the tissues as well as on body surfaces. A *germicide* is a substance which destroys germ life. An *antiseptic* retards or prevents the growth of septic organisms. *Asepsis* refers to a technique that avoids the introduction of viable organisms. *Sterile* means free from microorganisms or spores. A *disinfectant* is an agent that destroys disease organisms. An *antibiotic* is a substance initially elaborated by one organism and capable of interfering with the growth of another.

Define and illustrate the terms obligate, pleomorphous, and sporogenous. Name and explain the two varieties of chemotaxis.

Obligate: having no choice—obligate aerobe. *Pleomorphous* or *pleomorphic*—appearing in different forms under different conditions. *Sporogenous*—spore-forming.

Chemotaxis is the attracting or repelling force existing between ameboid cells, such as leukocytes (phagocytes), and food particles or bacteria. If the cells are attracted to the food particles, the term *positive* chemotaxis is used; if they are repelled, *negative* chemotaxis.

Define the following bacteriologic terms: strict parasite, spore, flagella, and mycelium.

A *strict* or *obligative parasite* is an organism that feeds exclusively on living organic matter. *Spore:* a small, oval, highly refractive body which appears in the protoplasm of bacteria when the conditions of growth cease to be favorable and which is capable, in a suitable medium, of developing into a bacterium. *Flagella:* delicate, hairlike projections of bacteria which serve as organs of locomotion. *Mycelium:* the growing or vegetative portion of a fungus (mold).

What is essential to the life of pathogenic bacteria?

A suitable temperature, generally at or near that of the body; generally, free or available oxygen; nutrient of a proper kind, containing both organic and inorganic material; a slight degree of moisture; a medium of slightly alkaline reaction; and rest. Some bacteria grow only in the presence of oxygen—obligative aerobes; some only in the absence of oxygen—obligative anaerobes; most pathogenic bacteria grow as well without as with oxygen—facultative anaerobes.

Give the functions and the products of bacteria.

Functions: Absorption, respiration, excretion, growth, motion, and reproduction.

Products: Fermentation—alcohol, acetic, lactic, and butyric acid; nitrogen metabolism—decomposition of nitrogenous substances with a variety of products; pigment (chromogenesis); gases—CO_2, H_2S, NH_3, odors; disease (pathogenesis); acids; aromatic compounds—indole; phosphorescence; reduction of nitrates and formation of ammonia and nitrogen.

Name the different modes by which bacteria propagate.

By direct or binary division or fission.

What is a pure culture?

A growth consisting exclusively of one species of bacteria.

Discuss symbiosis with special reference to pathogenesis.

The virulence of bacteria is sometimes increased and sometimes diminished by the association in culture of other species of bacteria.

How do we determine whether a certain organism is or is not the cause of a disease?

To prove that an organism is the cause of a given infection, certain conditions must be fulfilled. These are known as Koch's postulates:

(1) The organism must always be found in the lesions of the disease in numbers and under conditions that seem reasonably adequate to produce these lesions.

(2) It must be isolated in pure culture from the lesions, and its morphological and cultural characteristics carefully determined and recorded.

(3) The pure culture must produce in an animal the typical lesions of the disease.

(4) From this animal the organism must be recovered and proved to be the same as the injected organism, again determined by morphological and cultural studies.

(5) It must satisfy such serological requirements as may seem reasonably indicated. (The fifth has been added since the time of Koch.)

These criteria are now considered to be inadequate and, in some instances, too drastic; hence the addition of the fifth postulate. Some organisms are now commonly accepted as the cause of a given disease even though they do not satisfy all the postulates. On the other hand, a few are now questioned although at some time they had been accepted on the basis of these criteria. Finally, it may be impossible to cultivate the causative organism, although its presence in lesions may be demonstrable, e.g., leprosy bacillus.

Give the method of Gram's stain.

The smear is fixed with heat, then stained for one-half minute with a solution of crystal violet (*gentian violet*). Wash. Cover with Gram's solution (iodine 1 gm., potassium iodide 2 gm., water 300 cc.) for one minute. Wash. Apply 95 per cent alcohol until all but the thickest parts of the smear are decolorized, or for not more than two minutes. Wash. Counter-stain with *eosin*, *Bismarck brown*, or, preferably with *safranin*. Blot dry with filter paper. Violet-stained bacteria are gram-positive; red or brown-stained are gram-negative.

List the most important and most commonly encountered gram-positive and gram-negative pathogenic bacteria.

Gram-positive: *D. pneumoniae*, *Staphylococcus aureus*, Streptococci, *B. anthracis*, *Cl. tetani*, *Cl. perfringens*, *B. subtilis*, *M. tuberculosis*, *C. diphtheriae*, *M. leprae*, *Cl. botulinum*. Gram-negative: *N. meningitidis*; *N. gonorrhoeae*; *H. influenzae*; colon-typhoid-dysentery group; *Ps. aeruginosa*; *K. pneumoniae*; *H. dycreyi*; *P. pestis*; *Actinobacillus mallei*; *Bordetella pertussis*; *cholera vibrio*; *Brucella abortus*, *suis*, and *melitensis*; *P. tularensis*.

What are the most effective methods of sterilization?

Moist heat, dry heat, steam under pressure, burning and flaming, filtration, and light.

How would you sterilize culture media and why?

(*a*) By the *intermittent* or *fractional method* of steam sterilization. The culture medium is exposed to the action of steam in an Arnold or other suitable steam sterilizer for 15 minutes on each of 3 successive days. The first exposure kills all the fully developed bacteria; the bacteria that develop from spores in the course of the following 24 hours are killed by the next sterilization; and after the third exposure the medium is absolutely sterile. This method is employed for sterilizing culture media that contain components which are labile at 120°C. but stable at 100°C.

(*b*) By steam under pressure, usually at 15 lb. (121°C.) for fifteen to twenty minutes. For media whose components are not decomposed at this temperature.

(*c*) By bacteriological filtration, using Berkfeld candles, asbestos pads, or sintered glass. For thermolabile culture media.

Culture media are sterilized to destroy or remove associated contaminating organisms.

State the method of sterilizing the following: fluid culture media, dry test tubes, rubber stoppers, rubber gloves.

Fluid culture media, see previous question.

Test tubes are exposed to 160°C. for 1 to 1½ hours in a hot-air sterilizer.

Rubber stoppers and gloves are sterilized in nascent steam or boiling water, rendered slightly alkaline with sodium carbonate.

How would you proceed to find the number of bacteria per cubic centimeter in water?

Examine the specimen as soon after collection as possible. Make plate cultures on nutrient agar. After appropriate incubation, the number of developing colonies, each representing a single organism in the original specimen, is counted with the aid of a colony counter.

Describe in detail a bacteriologic procedure by which you could determine the fecal contamination of a water supply.

Fecal contamination is revealed by the presence of *E. coli*. Tests for this organism are made by inoculating appropriate amounts of the water sample into lactose broth. The presence of gas after incubation is presumptive evidence of the presence of *E. coli*. Confirmation is brought about by plating the lactose broth cultures on media that are selective and differential for *E. coli*. Final proof is based on isolation of pure cultures and identification by morphological, biochemical, and staining reactions.

Define ptomaines and leukomaines.

Ptomaines are basic organic compounds, resembling vegetable alkaloids, resulting from fermentative and putrefactive changes in the body set up by metabolic activities of *bacteria.* Examples: Cadaverin, putrecin, methylamine. They are found in spoiled meat, canned meat, sausages, stale milk and milk products, cheese, ice cream, custards, etc., and in fish, mussels, and other shellfish.

Leukomaines are basic chemical compounds, closely resembling the vegetable alkaloids, produced by the metabolic activities of the *organism.*

Discuss the role of antibiotic susceptibility tests in the treatment of infectious diseases.

One of the most important criteria for the successful use of the antimicrobial agents in combating infections is the isolation, identification, and determination of in vitro relative susceptibility of the etiological agent to the various drugs. It is true that in most instances the clinician can prescribe the appropriate specific antimicrobial agent as a result of an accurate history and thorough physical examination, without recourse to susceptibility testing. Nevertheless, on many occasions he is confronted with problems in which susceptibility tests can be helpful. It has been shown that there is variation among different genera of microorganisms with respect to their response to the activity of these agents, as well as variation among individual strains within a specified genus. In addition, sensitive organisms can develop resistance to antimicrobial agents under appropriate conditions, and the in vitro microbiological studies serve as the signal which indicates trends of changes of sensitivities and development of cross resistance to these drugs. Furthermore, the susceptibility tests can be of help in alerting the clinician to the probable development of a superinfection as a coincident complication of therapy, and also in the evaluation of activity of antimicrobial combinations. This is not meant to convey the impression that such testing is infallible, but it is generally agreed that, by and large, the anticipated clinical results as predicted by in vitro tests correlate well with those actually occurring in the clinic.

What is meant by the terms antimicrobial "resistant" and "susceptible"?

The clinical distinction between "resistant" and "susceptible" should be made with reference to the drug concentration obtainable in the blood of patients receiving some dosage of the same drug. For example, a dosage schedule which produces blood concentrations below those that are necessary for inhibition, as indicated by in vitro tests, automatically labels the infecting organism as "resistant." However, if, as a result of increased dosage or some other means (benemid with penicillin), the blood levels are elevated beyond the in vitro inhibiting concentration, the same organism is now designated as "susceptible." Hence, for clinical purposes, it is not necessary to know the definite concentration required for inhibition as long as it is less than the concentration attainable in blood with prescribed dosages.

Differentiate bacteriostatic and bactericidal agents.

In many instances, the selection of an antimicrobial agent is determined by the reputation which it has acquired as being either a static or a lethal agent, although in practice it is often extremely difficult to distinguish between bacteriostatic and bactericidal effects. Strictly speaking, the term "bacteriostasis" should apply only to those situations in which there is no change in the number of viable organisms during the time of exposure to an inhibiting compound, although, when their reproductive process is retarded, the organism may readily die of starvation or senescence and, after an appropriate lapse of time there may be a gradual but significant decrease in total numbers. Bactericidal activity is usually interpreted as referring to a situation where there is a rapid destruction of organisms, resulting in a diminution of their number. Therefore, it would seem that the sole valid distinction between bacteriostatic and bactericidal effects rest on the rate at which bacterial numbers decline, the rate being greater with bactericidal than with bacteriostatic agents. Since all antibiotics can be either bacteriostatic or bactericidal, depending on their concentration, these terms, from a clinical standpoint, are utilized in defining the activity of antibiotics under those conditions of concentration which can be obtained in the body. In the case of some antibiotics, even under conditions of maximal dosage, the blood and tissue levels attainable are such that at best they can manifest only a static activity. On the other hand, agents such as penicillin and streptomycin may, under conditions of ordinary dosage, produce concentrations which can exert a lethal effect and consequently are referred to as bactericidal agents.

For the majority of antibiotic therapeutic problems, it is not necessary for the clinician to know either the bacteriostatic or bactericidal susceptibility of an organism. Certain classes of organisms (*Streptococcus pyogenes,* alpha hemolytic streptococci, pneumococcus, gonococcus, meningococcus, and *Haemophilus* organisms) have been shown to be consistently susceptible to all known indicated antibiotics. On the other hand, there are certain groups of organisms (staphylococci, *Salmonella,* enterococci, *Escherichia, Shigella, Klebsiella,* paracolon, proteus, and *Pseudomonas*) that have been shown to be naturally resistant to most, or nearly all, of the available antibiotics. It is with diseases in which these organisms are involved that the clinician usually requires the assistance of in vitro susceptibility studies and may, from time to time, require information as to the bacteriostatic and bactericidal concentration of an antibiotic.

What factors may contribute to the discrepancy between in vitro susceptibility tests and clinical results?

(*1*) *Factors Influencing the Antibiotic:* Antibiotic activity is affected by physical and chemical factors that are variable according to the type and composition of culture media and may differ in the body fluids, tissues, and blood; since the population of specific organisms upon which the antibiotic acts is usually larger and denser in vitro than in vivo, the chances for development of factors within the medium that may inactivate the antibiotic (production of penicillinase) are greater in vitro. Thus, sensitivity tests carried out with a large inoculum of the bacteria may differ from results that are obtained with a smaller inoculum.

(*2*) *Factors Concerning the Organism:* The chance of survival is better in a large rather than in a small inoculum. The various immune mechanisms of the body play an important role, especially in the case of bacteriostatic agents.

(*3*) *Unexplained Factors:* For example, in the test tube chlortetracycline is more active than chloramphenicol against *Salmonella typhosa,* whereas the drug of choice for typhoid fever is chloramphenicol. From the above, it is apparent that microbiological susceptibility tests are of value primarily as general qualitative guides—namely, to distinguish the susceptible from the resistant organisms.

(a) Define bacteriostasis. (b) How is bacteriostasis accomplished?

(*a*) The inhibition of growth and reproduction of bacteria.

(*b*) By refrigeration, drying, pickling brines, and heavy sugar syrups. In laboratory work various aniline dyes are employed. The sulfonamides and antibiotics are bacteriostatic in action.

What is meant by phenol coefficient?

The efficiency or strength of a disinfectant is generally stated as its phenol coefficient. The dilution of disinfectant having the same killing power as 1 per cent phenol in the same length of time against standard strains of test organisms, divided by 100, gives the phenol coefficient.

Name and give the distinguishing morphologic and staining characteristics of two organisms that may infect man by means of contaminated water or milk.

(*a*) *Brucella abortus*—short slender, pleomorphic bacilli, nonmotile, nonsporulating, growing best microaerophilically; gram-negative. (*b*) *Mycobacterium tubercŭlosis* var. *bovis*—short, thick, solidly staining bacillus, gram-positive, acid- and alcohol-fast; growing best on egg- or glycerol-containing media; nonmotile and nonsporulating.

Name three members of the group of pathogenic, anaerobic, sporulating bacteria and the diseases they cause.

Clostridium perfringens (gas gangrene); *Clostridium tetani* (tetanus); *Clostridium botulinum* (botulism).

Give an account of the Welch bacillus.

Discovered (by isolation from cadavers) independently by Welch and Nuttall in America, Fränkel in Germany, and Veillon and Zuber in France. It was first called *Bacillus aerogenes capsulatus*, but the designation *Clostridium perfringens* is now generally used in America. In wounds it ferments the muscle sugar, producing gas in the tissues ("gas gangrene"); hence it is also called the *gas bacillus*. It is a short, straight or slightly curved rod of variable length and thickness with square ends, encapsulated, nonmotile, and occurring singly or in pairs. It grows best at body temperature and under anaerobic conditions. Spores are produced only in the absence of fermentable carbohydrate, e.g., dextrose. The best media are cooked meat and milk. It is stained by the aniline dyes and is gram-positive. It acts on sugar and starches, very little on proteins. Rapid fermentation of milk lactose in milk, attended by the well-known "stormy" fermentation is diagnostic of the bacillus. Inoculation of milk with material from a wound will establish the diagnosis in twelve to eighteen hours. The production of gas gangrene in wounds containing *Cl. perfringens* depends on the virulence of the strain, the amount of dead tissue, and anaerobic conditions. The bacillus has been found in 80 per cent of wounds examined, but only 10 per cent developed gas gangrene.

Describe the pneumococcus, and give its characteristic experimental reaction.

An oval coccus, usually occurring in pairs, and sometimes forming chains of four or five units. Pneumococci obtained from excretions or diseased tissue have a lance-shaped extremity and are surrounded by a *capsule*, which in the presence of type-specific serum shows the Neufeld phenomenon of Quellung. The organism is nonmotile, has no flagella, and does not form spores. It stains by Gram's method, being thereby differentiated from the gonococcus and the meningococcus. Milk is rapidly coagulated. It is a facultative anaerobe. It can be differentiated from streptococci by the Neufeld reaction and by its solubility in bile or bile salts.

Where is gonococcus usually found? Describe its characters. Give specifically a method of staining it.

The gonococcus attacks cylindric epithelium and is usually found in discharges from the urethra, conjunctiva, and rectum. It does not attack flat epithelium; hence gonorrhea of the mouth or nasal passages does not occur. The gonococcus is a coffee-bean–shaped diplococcus, usually found intracellularly in pus cells. It requires special media for its cultivation. No stain is specific, but, for a diagnosis, it is best to stain by Gram's stain. Gonococci are gram-negative.

What special culture medium is required for the growth of the gonococcus? Give the pathogenicity of the gonococcus.

Proteose peptone agar containing starch and enriched with whole blood or hemoglobin together with a sterile yeast concentrate prepared so as to preserve thermostable and thermolabile growth accessory factors, e.g., glutamine, coenzyme (V factor), and cocarboxylase.

The gonococcus is always found in the purulent discharge from gonorrheal inflammations anywhere in the body. It is never an inhabitant of normal mucous membranes. The gonococcus is said to have a tendency to remain latent in the tissues, retaining its pathogenic power, and to renew its activity after a long period of latency.

Describe the tubercle bacillus.

A straight, rod-shaped organism, 1.5 to 3.5 μ long and about 0.5 μ thick, beaded, often occurring in pairs or groups. It is *acid-fast* and *alcohol-fast*, i.e., stains with difficulty (carbol fuchsin), and retains the stain with great tenacity, despite vigorous attempts at decolorization with mineral acid and alcohol.

Explain pasteurization of milk and describe the procedure.

The creaming properties of milk are not impaired by momentary heating to 165°F. if the temperature is immediately reduced to 145°F.; hence milk or cream may be heated to at least 142°F. for 30 minutes without impairing its usefulness.

Hemolytic streptococci and diphtheria bacilli are killed by momentary exposure to 129°F.; typhoid bacilli by momentary exposure to 141°F. and by heating to 132°F. for 30 minutes.

Bovine tubercle bacilli are killed by exposure to 138°F. for 30 minutes.

Pasteurization consists in heating milk to 143° or 144°F. for 30 minutes and is the most effective method of preventing milk-borne infection. The milk is immediately bottled after pasteurization and the bottles kept in a cool place; or the pasteurization may be done in the final containers, which are then immediately sealed.

With what bacteria found in milk may the tubercule bacillus be confounded?

The butter bacillus, *Clostridium butyricum.*

State where the smegma bacillus is found, and give the mode of differentiating it from the bacillus of tuberculosis.

Beneath the prepuce of man and between the labia of woman. It is differentiated from the tubercle bacillus by the fact that it is decolorized by absolute alcohol, and does not produce tuberculosis when inoculated into an animal, as it is a nonpathogenic organism.

Describe the leprosy bacillus.

A straight, slender rod, with rounded ends, a little shorter than the tubercle bacillus, to which it bears a close resemblance both morphologically and tinctorially. It is nonmotile and does not form spores. It is readily stained with aniline dyes and is not decolorized by mineral acids. It has never been grown in artificial culture media. Leprosy cannot be transmitted to animals by inoculation.

Give the origin, morphology, properties, and growth characteristics of *Clostridium septicum.*

A motile, sporogenic, anaerobic, liquefying, nonchromogenic, pathogenic organism found in soil and in animal intestines. It measures 2 to 10 μ by 0.8 to 1 μ.

Describe the Klebs-Löffler bacillus. How do you stain for it? What disease does it cause?

The shape is very inconstant: the bacilli may be straight or curved, uniform or irregular in size; they usually occur singly, with a tendency to parallelism. The organism is nonmotile. Löffler's alkaline methylene blue is the stain usually employed, under which conditions the organism does not stain uniformly but shows alternate bands of stained or unstained material, as well as metachromatic granules. The latter can be differentially stained by means of Bech stain. The organism elaborates a powerful exotoxin and is the cause of diphtheria.

Define fungus. Name the criteria upon which identification is based.

A fungus is any one of a class of vegetable organisms that does not contain chlorophyll, reproduces through the production of spores, and in the vegetative phase produces septate or nonseptate mycelium. A fungal spore is a specialized cell which under suitable conditions germinates into a filamentous process called a hypha. Mycelium is a mass of hyphae which have branched, rebranched, and intertwined.

Fungus identification is based on morphology (*a*) macroscopically on the type of colony, (*b*) microscopically on the type of spore produced.

Name and describe the three principal colony types of medically important fungi; cite an example of each.

(*a*) Yeast type: soft, bacteria-like; and composed of single-celled budding forms—*Cryptococcus.* (*b*) Yeastlike type: soft, bacteria-like; and composed of single-celled budding forms on the surface and hyphae that penetrate the medium —*Candida.* (*c*) Filamentous type: composed of branching hyphae, some of which penetrate the medium; vegetative mycelia, some of which project from the surface (aerial mycelium) and are sometimes referred to as reproductive mycelia when giving rise to, spores—*Blastomyces.*

Name the fungal genera which are most frequently encountered in dermatomycoses. State which parts of the body are most frequently affected.

GENUS	AFFECTED AREA
Trichophyton	Skin, hair, and nails
Microsporum	Skin and hair
Epidermophyton	Skin and nails

Name the laboratory procedures useful in identification of fungi.

(1) *Direct Microscopic Examination:* Specimens stained by Gram's and Wright's stains. Iron-alum hematoxylin and periodic acid preparations give excellent results with sectioned material.

(2) *Cultural Methods:* (*a*) Sabouraud's agar: for primary isolation of dermatophytes and *Candida;* (*b*) corn meal extract agar: for specific recognition of *C. albicans;* (*c*) blood agar with added penicillin and streptomycin: primary isolation of *Histoplasma, Coccidioides,* and *Blastomyces;* (*d*) blood agar; *Nocardia;* (*e*) thioglycollate broth: *Actinomyces.*

(3) *Animal Inoculation:* The mouse is the most useful animal, being susceptible to *Blastomyces dermatitidis* and *brasiliensis, Coccidioides immitis, S. schenckii, C. hominis, H. capsulatum.*

Give the characters of *Bacillus anthracis,* ray fungus.

B. anthracis: 2 to 4 μ in length and about 1 μ wide, with a tendency to form long chains; aerobic, nonmotile, and forming oval central spores. Stains with aniline dyes and by Gram's method. Cultivated easily on all kinds of media between 14° and 43°C. On gelatin plates characteristic opaque, grayish colonies with irregular borders develop in twenty-four hours. Liquefies gelatin slightly.

Ray fungus or *Actinomyces bovis:* Appears in lesions as small, yellow granules from 0.5 to 2 mm. in diameter, consisting of a central granular mass from which radiate a large number of club-shaped threads. Stains with aniline dyes and by Gram's method; anaerobic to microaerophilic. The organism is not a mold, although it produces a true mycelium which fragments into elements of irregular size and may show angular branching. Causes actinomycosis.

Give the morphology of the tetanus bacillus; what are its toxins?

From 4 to 8 μ long, and about 0.5 μ wide, easily recognized by its "tennis racquet" shape, which is due to the terminal location of the spore. The enlargement at one end contains a spore. It has no flagella, usually occurs singly, is anaerobic and gram-positive. Hemotoxin and neurotoxin (tetanospasmin).

How does the tetanus bacillus produce its effects? Upon what theory is tetanus antitoxin administered?

By the production of toxins. The rationale is analogous to immunization against diphtheria. The aim is to neutralize the effect of the toxin in the body by the administration of an antitoxin. The linking of toxin and antitoxin of tetanus in the body is a subject still under discussion. While the toxin presumably passes directly to the nerve paths, the antitoxin injected subcutaneously is taken up by the blood vessels by way of the lymphatics. A fatal dose of the toxin already taken up by the nerves cannot, therefore, be neutralized by antitoxin introduced subcutaneously; and substance must be injected directly into the nerves. The principal value of tetanus antitoxin at present is prophylactic—its injection in cases of dirty wounds that present the probability of tetanus infection.

Describe the typhoid bacillus (*S. typhosa*) and state (*a*) whether aerobic or anaerobic; (*b*) saprophyte or parasite; (*c*) facultative, strict or obligatory; (*d*) the manner of its action; (*e*) where found in the body and how eliminated.

(*a*) A small thick rod, from 1 to 3 μ long and 0.5 to 0.8 μ wide; is motile and does not form spores. Facultative anaerobe with strong aerobic tendencies. (*b*) Both. (*c*) Facultative. (*d*) The organism enters the body through the digestive tract and, during the incubation period, multiplies in the lymphoid tissue of the wall of the small intestine and regional lymph nodes. From here the bacilli make their way to other portions of the body, especially the spleen, liver, kidneys, gallbladder, bone marrow, and mesenteric lymph nodes. (*e*) The bacilli are found in the intestinal ulcers, the mesenteric lymph nodes, spleen, liver, kidneys, and occasionally the bladder. They are eliminated in the feces and sometimes the urine, especially during convalescence.

(*a*) Describe in detail the examination of sputum for tubercle bacilli. (*b*) How would you make a bacteriologic diagnosis of diphtheria?

(*a*) The small "cheesy" particles in the sputum are selected for examination. One of these is picked up with a platinum loop or a toothpick and thinly spread on a slide. After drying in the air, fix the preparation by passing it 3 times through the flame. Flood slide with carbol fuchsin solution. Steam gently over a flame for five minutes, wash with water, decolorize with a mixture of 3 ml. concentrated HCl in 95 per cent ethanol until washings are colorless. Counterstain with Löffler's methylene blue for 30 seconds, wash with water, dry, and examine under oil immersion.

(*b*) A diphtheria diagnosis outfit, such as most boards of health supply, comprises 2 culture tubes containing blood serum, a swab or inoculator in a sterile glass tube, and a wooden tongue depressor. The suspected throat or diphtheritic membrane, if present, is rubbed with the swab and one culture tube inoculated. A second swab is taken of the nasopharynx and similarly used to inoculate the second culture tube. The culture tubes with the inserted swabs are placed in the incubator and in from 9 to 12 hours small white colonies make their appearance, from which smears are prepared and stained.

Describe in detail the bacteriologic diagnosis of glanders.

Inoculate exudate or biopsy material to blood agar plates. Incubate twenty-four to forty-eight hours. Make Gram stain smears and observe gram-negative bacilli. Smears stained with alkaline methylene blue reveal unevenly stained bacilli. Confirm by agglutination test with type specific antiserum. Animal inoculation is more reliable. Inject the suspected material into the peritoneal cavity of a male guinea pig. If *Actino-*

bacillus mallei is present, the testicles soon break down and may discharge through the skin. On killing the animal, the tunica vaginalis is found full of fluid pus, from which pure cultures can be obtained.

Give the bacteriologic diagnosis of actinomycosis.

Sputum or exudate is spread in a sterile Petri dish and examined for the presence of characteristic "sulfur granules." These are transferred to a slide and crushed under a coverslip. Microscopic examination reveals round or lobulated masses of intertwining mycelia. The ends of the hyphae radiating peripherally from the mycelial mass may or may not be clubbed. Cultures are best prepared from such "granules" or pus inoculated into solid or semisolid media containing blood and incubated anaerobically.

Give the bacteriologic findings in conjunctivitis.

The more common bacteria are: *D. pneumoniae, N. gonorrhoeae, Moraxella lacunata, H. influenzae, E. coli, C. diphtheriae,* and streptococci.

What are rickettsia bodies and what diseases are caused by them?

They are intermediate in properties between bacteria and viruses and possess some of the properties of both: (1) not cultivable on media devoid of living cells or tissue; (2) visible with ordinary microscopes, but smaller than bacteria; (3) unable to pass through filters which withhold bacteria. The following diseases are caused by rickettsiae: spotted fever group, typhus fever group, tsutsugamushi group (scrub typhus), and the Q fever group.

Describe two methods by which insects transmit disease to man.

(1) *Mechanical:* as illustrated by transmission of typhoid and dysentery bacilli from infectious feces on the legs of flies which crawl on food etc. (2) *Biological:* as seen in the spread of malaria by bites of infected mosquitoes.

List the important properties of viruses.

(1) They are ultramicroscopic. (2) They pass through the finest filters. (3) They grow only within cells, often only within certain types of cells and in certain species of animals. They can be grown only in media containing living cells or in the membranes of the developing egg embryo. (4) In many viral infections inclusion bodies are seen in the infected cells. (5) Many viruses lie dormant in tissues for long periods of time, producing neither symptoms nor lesions. Under these conditions, however, a virus may be highly virulent for a host of a different species; for its original host if resistance is lost; or, for a fetus which is being carried in utero. (6) Viral infections tend to pave the way for bacterial infection. (7) Immunity of high degree and long duration characteristically follows viral infections except the common cold, influenza, and herpes simplex. (8) Many viruses are transmitted to man by insect vectors. (9) Viral infections in general do not respond to antimicrobial agents. This is probably due to their intracellular location and metabolic dependence on their host cells.

What are "elementary bodies"? Mention a few diseases in which they have been observed.

Elementary bodies are small particles seen in the lesions of many virus infections and are considered to carry the infectious property of the virus. Variola, varicella, molluscum contagiosum.

Define "inclusion body." How many types are known? In what diseases do they occur?

Structures seen in cells parasitized by viruses. They may be in either the nucleus or cytoplasm. They are best demonstrated by Mann's eosin methyl blue or Giemsa stain. Nuclear inclusion bodies are seen in herpes, yellow fever, and chicken pox. Cytoplasmic inclusion bodies are seen in rabies, variola-vaccinia, and ectromelia.

By what laboratory methods may rabies be diagnosed?

The virus of rabies is known to reside in the nervous tissues of the infected animal. An emulsion is made by rubbing up 1 cm. of dried spinal cord from an animal dead of rabies with four or five times its bulk of bouillon. If this emulsion is injected into the veins of an animal, the symptoms of rabies make their appearance and the animal dies.

The finding of the globoid, nucleated, so-called "Negri bodies" in the brain of the suspected animal is practically pathognomonic. The bodies are found chiefly in the hippocampus major and in the Purkinje cells of the cerebellum. In stained sections the bodies are found within the cytoplasm of the nerve cells as small oval bodies, stained pink, varying in size from 1 to 27 μ in diameter. Three or four may be found in a single cell.

What are protozoa? Name three pathogenic protozoa and the diseases they produce.

A protozoon is an animal organism composed of a single cell. *Plasmodium malariae* (quartan malaria), *Endamoeba histolytica* (amebiasis), *Trypanosoma gambiense* (African "sleeping sickness").

Name the malarial parasites and describe a "trophozoite."

The malarial parasites are (1) *Plasmodium vivax,* the cause of benign tertian malaria; (2) *Plasmodium malariae,* the cause of quartan malaria; (3) *Plasmodium falciparum,* the cause of estivo-autumnal malaria; and (4) *Plasmodium ovale,* a species not yet introduced into the United States.

A full-grown malarial parasite is composed of *protoplasm,* which is circular when at rest and irregular in outline when the pseudopods are extended. This cytoplasm is stained blue by all the ordinary blood stains. Eccentrically placed there is a clear space, which represents the *nucleus.* At one side of the clear space, when a polychrome methylene blue stain has been employed, there is a dark or purplish-red spot which is the *chromatin.* Embedded in the protoplasm of the parasite there are numerous pigment granules, which are in reality altered hemoglobin varying in color from yellow to brown. In a fresh preparation, the pigment is seen to be in active motion and the pseudopods can be seen actively extending and retracting.

State in detail how you would (a) detect malarial organisms in stained blood films, (b) distinguish between the quartan and estivo-autumnal parasite.

(*a*) Cleanse the skin surface to be pricked, preferably of the finger, with a pledget of cotton moistened with alcohol and then wipe dry. Using a lancet, puncture the skin deeply enough so that blood flows freely under gentle pressure. Wipe off the first blood that exudes. The size and number of drops of blood to be taken for blood films will depend on

(*b*)	*P. malariae*	*P. falciparum*
Infected cell	Multiple infection rare.	Multiple infection common.
Small trophozoite	Signet ring with heavy chromatin dot.	Small cytoplasmic circle, achromatic dots, marginal and bridge forms frequent.
Growing trophozoite	Chromatin round or elongated, cytoplasm compact. Dark-brown pigment granules.	Resembles *P. malariae,* but considerably larger, pigment lighter in color and less conspicuous.
Mature schizont	6 to 12 in a rosette or cluster. Practically fills normal-sized cell.	8 to 24 very small. Rarely found in peripheral blood. Fills about ⅔ of normal-sized cell.
Macrogametocyte	Dark-blue homogenous cytoplasm; abundant dark-brown pigment; circular or ovoid.	Deep-blue cytoplasm; single dark-red chromatin mass near center. Crescented or sausage shaped.
Stages in peripheral blood.	All.	Ring form trophozoites and gametocytes.

whether a thin or thick film is desired. A thin film is ideal for the study of morphology of the parasite and for identification of stages and species of parasites when infection is heavy. A thick film is preferred in cases of spare or scanty infection.

Distinguish between (a) *Leishmania donovani,* (b) *Leishmania tropica,* and (c) *Leishmania brasiliensis.*

(*a*) Causes kala-azar or visceral leishmaniasis. (*b*) Causes cutaneous leishmaniasis or oriental sore. (*c*) Causes mucocutaneous leishmaniasis or espundia. Diagnosis and differentiation are based upon examination of stained blood films and tissues, specific agglutination tests, Napier's aldehyde test, Chopra's antimony test and Sia's precipitative test and complement-fixation tests.

How do you diagnose an infestation with *Dibothriocephalus latus?* What is the source of the agent and how does man become infested?

Examination for ova; occasionally segments of this flatworm will be seen in the feces. The agent is parasitic for fish, notably pike, grayling, and certain trout. Man becomes infested by ingesting infected fish.

(a) Name 5 organisms commonly found on normal mucous membranes of man, (b) By what pathways may such organisms reach other sites wherein they may induce disease?

(*a*) *Staphylococcus aureus,* anaerobic streptococci, *E. coli, Bacteroides, Ps. aeruginosa.* (*b*) Impairment of any of the several factors contributing to normal resistance, e.g., trauma resulting in cellular and tissue damage, malnutrition, intoxication, acute infections, endocrine imbalance.

Name two parasites responsible for infestations in which skin tests have practical value.

Echinococcus granulosus (Casoni test), *Trichinella spiralis.*

State what further bacteriologic methods should be employed if direct examination of the sputum from a case of suspected pulmonary tuberculosis fails to reveal acid-fast organisms.

Concentration and culture of sputum, gastric washings, animal inoculation.

Name a pathogenic helminth transmitted to man by the bite of an insect and mention the disease it causes.

Wuchereria bancrofti (*Filaria bancrofti*), transmitted by species of *Culex, Aedes,* and *Anopheles* mosquitoes, causing filarial elephantiasis.

SEROLOGY AND IMMUNOLOGY

Describe the various types of immunity.

Natural: An immunity observed in one species to diseases in other species, such as human immunity to hog cholera.

Acquired: An immunity on the part of an individual to diseases which may attack other individuals of the same species. Acquired immunity may be active or passive. Active immunity may be acquired by an attack of a disease such as measles, artificially by vaccination (smallpox), or by injection of a toxin (diphtheria). Passive immunity is acquired by the injection of antibodies (immune serum).

Congenital: Immunity at birth to scarlet fever occurring in some persons.

Racial: Relative immunity, as yellow fever in Negroes.

What are antibodies?

Antibodies are humoral globulins produced by certain tissue cells, which tend to react with antigens in some observable way. When antibodies are produced in large quantities they invade the blood stream and there they can be demonstrated by various laboratory procedures.

Discuss the various types of antibodies.

Antitoxins, which neutralize toxins, as in diphtheria. *Lysins,* which cause the dissolution of antigen. *Opsonins* and *bacteriotropins,* which change the invading organism so that it is more easily destroyed by the phagocytes. *Agglutinins* and *precipitins,* which cause the clumping and precipitation of the homologous antigen.

What are antigens?

Antigens are proteins or carbohydrates which, when introduced parenterally into a species of animal other than that from which they were derived, stimulate antibody production. They may gain entrance to the body naturally, as by an infectious disease, or may be injected into the body for the purpose of gaining immunity.

State what is meant by (a) first order, (b) second order, and (c) third order antibody. Give an example of each.

(*a*) Antibodies with one combining portion only—antitoxins.

(*b*) Antibodies which in addition to a combining portion possess a portion having enzymatic activity—agglutinins, precipitins, opsonins.

(*c*) Antibodies possessing two combining portions, one reacting with antigen, the other with complement—lysins.

Differentiate between the terms serum and vaccine as used immunologically.

The term "serum" is used for preparations in which the blood serum of immunized animals is given to confer passive immunization. The term "vaccine," used originally for immunization to smallpox, is now used for a preparation or suspension of attenuated or killed organisms which produces active immunization by inducing the formation of antibodies.

Name several seroflocculation tests for syphilis and describe one briefly.

VDRL, Kahn, Kline, Hinton, Mazzini, and Eagle.

The Kline test is a microscopic test for the presence of syphilis and may be applied to the blood. The test consists in mixing cholesterolized antigen suspension and inactivated serum on a slide and noting the formation of precipitates under the microscope.

Discuss biologic false positive tests for syphilis (BFP).

In recent years it has been apparent that many diseases can produce temporary or permanent biological false-positive tests for syphilis (BFP). Common causes are: upper respiratory infections, infectious mononucleosis, smallpox vaccination "takes," malaria, systemic lupus erythematosus. Hence, a diagnosis of syphilis should never be made on the basis of one positive serological test (STS) without confirmatory evidence of syphilis. In the absence of clinical or case-history confirmation, the STS should be repeated at monthly intervals for three months. If the STS remains positive at the end of this period, a *Treponema pallidum* immobilization test (TPI) is advisable. This test is apparently highly specific; a positive reaction can be considered as a definite serological indication of syphilis, in that the serum of persons with syphilis contains a substance that immobilizes *Treponema pallidum.*

Mention a biologic test for the presence of infection with gonococcus and discuss its clinical value.

Gonococcus complement-fixation test. The technique is similar to that of the Wassermann test for syphilis, but employs different antigen.

Acute Urethritis: A positive reaction is seldom obtained during the first four to six weeks of an acute anterior or posterior urethritis, unless complications are present.

Chronic Urethritis: In ordinary chronic cases with mild prostatic infection, the reaction is positive in from 30 to 40 per cent. With marked involvement of the prostate and epididymitis, it is positive in from 50 to 80 per cent of the cases.

The reaction may persist for several weeks after a clinical cure has been accomplished, and the patient should be kept under observation until the reaction disappears, which is usually in two to three weeks. He should not marry so long as a positive reaction is obtained.

Gonorrheal Arthritis: The test is particularly valuable in this condition, being found positive in from 80 to 100 per cent of the cases.

In women the test is rarely positive until the infection has invaded the cervical canal. It is positive in about 60 per cent of cases of pyosalpinx.

In acute and chronic vulvovaginitis of children a positive reaction is occasionally obtained.

In general, the value of a positive reaction is much greater than that of a negative test.

Describe the Wassermann reaction.

A complement-fixation reaction consisting of a nonspecific antigen prepared by extracting normal beef heart and fortifying it by the addition of cardiolipin, cholesterol, or lecithin; fresh complement in the form of pooled normal guinea-pig serum; patient's blood serum acting as amboceptor; and a hemolytic system consisting of sheep red cells (antigen) and rabbit serum immunized against sheep red cells (hemolysin). The antigen, complement, and patient serum system is incubated at 37°C. for 30 minutes, and the hemolytic system is then added to it. If the patient has syphilis, reagin in his blood serum will bind complement. To demonstrate this binding of complement, the hemolytic system is added, no complement is available and so no hemolysis will result, and the red cells will settle to the bottom of the tube (*positive Wassermann*). If the patient does not have syphilis, complement will be available and hemolysis will result (*negative Wassermann*).

Name several diseases besides syphilis in which the Wassermann reaction is often positive.

Yaws, relapsing fever, leprosy, and malaria.

Describe the Widal agglutination test and its diagnostic value for typhoid fever.

The patient's blood is centrifuged in order to obtain serum. Seven tubes are placed in a rack. One tenth of a cc. of blood serum and 0.9 cc. of physiological saline are pipetted into the first tube and 0.5 cc. of saline into each of the other tubes. Of the contents of tube No. 1, 0.5 cc. are transferred to tube No. 2; then 0.5 cc. of No. 2 to No. 3 and so on. The 0.5 cc. from the next to the last tube is discarded, the last tube acting as a control. Dilutions thus are 1:10, 1:20, 1:40, 1:80, 1:160, 1:320. To each tube, 0.5 cc. of a suspension of killed S. *typhosa* is added, thus doubling the dilutions. The tubes are shaken and are placed in an incubator for 8 to 12 hours. Tubes containing agglutinated bacteria at the bottom are considered positive. Agglutination in 1:40 or 1:80 dilution of serum or less has little significance, particularly during the early stages of the disease. The test should be repeated at weekly intervals to demonstrate either a four-fold rise or fall in titer. When positive, the test is of very great value unless there has been a previous attack of typhoid fever or the individual has recently been immunized with typhoid vaccine; the reaction is rarely negative throughout the course of the malady, but it may not appear until late. The fifth day is the earliest that the reaction usually appears. A negative reaction does not definitely exclude typhoid fever, but is nevertheless of considerable negative value. In rare cases of typhoid the reaction is persistently negative throughout.

What is the diagnostic value of the fluorescent-antibody test?

One of the relatively new immunological techniques is the use of the fluorescein-labeled antibody to identify various bacteria, such as *Haemophilus* *influenzae,* streptococci, *Escherichia coli,* and pertussis organisms.

Discuss the Weil-Felix test.

The Weil-Felix test is conducted in the same manner as the Widal test for typhoid fever, except that the O strain of Proteus X-19 bacillus is used as the antigen in place of S. *typhosa* of the Widal. A positive Weil-Felix reaction is indicative of one of the rickettsial diseases.

What is the Paul-Bunnell test and in what disease is it positive?

Heterophile antibody titration following absorption of patient's serum with antigen prepared from normal guinea-pig kidney and ox red cell. It is positive in infectious mononucleosis.

Define (a) Schutz-Charlton test, (b) Frei test, (c) chancroid antigen test.

Schultz-Charlton Test (Scarlet Fever Diagnostic): Scarlet fever streptococcus antitoxic serum is used in the performance of this test to differentiate the rash of scarlet fever from eruptions due to other causes.

Inject intracutaneously, in an area of rash, 0.1 to 0.2 ml. of the diluted antitoxin (containing 2,000 to 5,000 original neutralizing units). In scarlet fever, there will be partial or complete disappearance of the rash over an area 2 cm. or more in diameter; this occurs from 4 to 24 hours after the injection. This test is usually considered to be specific; no other rash fades in this manner.

Frei Test: This is a fairly specific test for past or present infection with the virus of lymphogranuloma venereum. Three types of antigen are in use: human antigen, obtained by appropriately preparing material aspirated from buboes; mouse-brain antigen; chick-embryo antigen. Recent work indicates that the latter is probably the most satisfactory. Controls must be used with both the mouse and the chick antigen to rule out protein sensitivity.

Inject 0.1 ml. of the Frei antigen intracutaneously on the flexor surface of the forearm; apply the control similarly, if indicated. The reaction is read after 48 to 72 hours. An inflammatory papule 7 mm. or more in diameter is a positive test.

A positive reaction can be obtained in about 95 per cent of cases within 7 to 10 days after the development of the adenopathy; it apparently remains positive throughout the life of that individual.

Chancroid Antigen Test (Ducrey Test): The test material is a saline suspension of Ducrey's bacilli (*H. ducreyi*). Inject 0.1 ml. of this material intracutaneously in the flexor surface of the forearm. The test is read after 48 to 72 hours. An inflammatory papule 7 mm. or more in diameter is a positive reaction. With minimal-sized papules the surrounding erythema must measure at least 14 mm. in diameter before the test is considered positive.

Give a general description of the action of agglutinins.

The serum of animals immune to a specific bacterium, as S. *typhosa* or *V. cholerae,* when added to a culture of the specific organism, produces the phenomenon known as agglutination (Gruber). The agglutinins, or agglutinating substances, first cause the bacilli to lose their motility; they then gather in clumps or bunches, and finally are observed as a flocculent precipitate. The phenomenon is seen in its most typical form in the Widal reaction of typhoid fever.

Define complement and amboceptor. Where are they found? What is their significance?

"Complement" (also called "alexin") is the name given to a group of proteins that are found in both normal and immune serum and that exhibit the property of combining with antigen-antibody systems. Amboceptor is a term first applied by Ehrlich to designate antibodies which lyse cells in the presence of complement. These amboceptors are specific for the antigen which has stimulated the cells of the body to their production. Complement and amboceptor working together combat and destroy the invading pathogens.

Complement is free in the blood serum and apparently cannot attack the cells without the cooperation of the specific amboceptor or cytolysin. Complement is very labile, deteriorates rapidly when allowed to stand for a few hours at room temperature, and is completely destroyed by heating to 56°C. for half an hour. In laboratory work it is obtained from guinea pigs.

Discuss the properdin system.

This system is viewed as an important factor in nonspecific resistance to infection. The amount of properdin in the blood appears to vary directly with general resistance to infection by certain bacteria, as well as by some viruses. Properdin, one of the components of the system, is a serum protein, the other components of the system being Mg^{++} and complement. The action of the system is nonspecific, like that of complement.

What is the complement fixation reaction and what is its significance?

The reaction whereby complement in the presence of an antigen and its homologous antibody will be bound. The reagents needed for its demonstration are: (1) An *antigen* that is specific for the disease under investigation. Usually the antigen is the organism known to be responsible for the disease (this is not true of the Wassermann test). (2) The inactivated blood serum of the patient who is being tested (immune bodies). (3) Complement (fresh guinea-pig serum). (4) Antisheep amboceptor (hemolysin). (5) A suspension of washed *sheep cells.* (6) Known positive and negative controls, i.e., sera of other patients. Failure to produce hemolysis indicates a positive reaction, complement fixation, and, conversely, hemolysis means a negative result. The test is used either to detect antibodies (as commonly employed for the identification of disease) or for the detection of an antigen in various research problems.

Describe the Davidsohn presumptive and differential test for heterophile antibody.

Washed sheep cells are added to serial dilutions of patient's serum and observed for evidence of agglutination after a suitable incubation period. Agglutination of erythrocytes is presumptive evidence of heterophile antibody. The test is suggestive of infectious mononucleosis when positive in a dilution of 1:112 or higher. The differential test is used to discriminate between the antisheep agglutinins associated with glandular fever and those associated with serum sickness. This is accomplished by absorbing the serum, before exposure to sheep erythrocytes, with antigen prepared from guinea-pig kidney and beef erythrocytes. The sheep cell agglutinins produced in infectious mononucleosis and serum sickness are completely absorbed by beef erythrocytes, while guinea-pig kidney antigen absorbs the Forssman antibody of serum sickness, but not the antibody of infectious mononucleosis.

Differentiate between cold agglutination, autoagglutination, panagglutination, and pseudoagglutination.

Cold Agglutination: Erythrocyte agglutination between 0° and 5°C., reversible at 37°C.

Autoagglutination: Agglutination of erythrocytes by the patient's own serum at room temperature.

Panagglutination: Agglutination of erythrocytes after being acted upon by bacteria (Huebner-Thompson phenomenon).

Pseudoagglutination: Rouleaux formation.

Mention the more important blood factors occurring in human erythrocytes.

Factors A, B, O, M, N, and Rh.

Mention the several blood groups and explain the rationale for the Landsteiner classification.

The blood of all humans can be classified into four groups, A, B, AB, and O. Subgroups of A have been recognized. Thus, Group A can be divided into A_1 and A_2. Similarly, Group AB may be subdivided into A_1B and A_2B. A_3 and A_3B have also been described, although these types are exceedingly rare.

The Landsteiner classification is based upon the existence or absence of agglutinogens (A, B, O) in human erythrocytes and the presence or absence of corresponding agglutinin (anti-A and anti-B) in the serum. Agglutinogens are antigens; agglutinins are antibodies. Contact between incompatible agglutinogen and agglutinin results in agglutination, more specifically iso-agglutination.

Define the Coombs' test, state the principle upon which it is based, name two types, and state under what conditions they are applicable.

A serological procedure to detect abnormally coated erythrocytes, abnormal agglutinins, and unusual blood factors.

Erythrocytes from patients with blood dyscrasias (particularly, acquired hemolytic anemia and erythroblastosis) may become coated in vivo with specific or nonspecific antibodies, many of which are not present in saline suspension. They can, however, be demonstrated in vitro in suitable protein diluents, such as albumin or globulin.

(*a*) Direct Coombs: to detect antibodies which have become fixed to a patient's erythrocytes in vivo, e.g., erythroblastosis fetalis, acquired hemolytic anemia. (*b*) Indirect Coombs: to detect circulating antibodies which coat, but do not agglutinate, saline-suspended cells. Examples of such antibodies are albumin agglutinins, incomplete antibodies, blocking antibodies, cryptagglutinins, etc. The indirect test is applied for the detection of Rh or other antibodies formed as a result of iso-immunization by pregnancy or transfusion. It is also helpful in performance of cross matchings for transfusion when the recipient may have antibodies that will not agglutinate the saline-suspended donor cells.

Describe the Donath-Landsteiner test and name the disease in which its use is indicated.

The Donath-Landsteiner test reveals the presence of an autohemolysin in blood serum which is active at temperatures of 0°C. or slightly above, but inactive at 37°C. The hemolysin is characteristically associated with paroxysmal hemoglobinuria. As a rule the patient's serum at the same time shows a strongly positive Wassermann reaction.

What is the Rh factor? Discuss its action.

The Rh factor is an antigen present in the blood (particularly in the cells) of 85 per cent of Caucasians and higher percentages of other races. The other 15 per cent do not possess the antigen and are *Rh negative*. The factor is passed on genetically as a mendelian dominant. Rh antibodies do not occur normally. They may develop in an Rh negative individual after the injection of Rh positive blood (usually by transfusion), or as the result of pregnancy in which the fetus was *Rh positive*. If they develop, the person is said to be sensitized.

Transfusion of Rh positive blood to a sensitized Rh negative woman will cause a reaction and increased sensitization; pregnancy in which the fetus is Rh positive may result in an erythroblastic infant and increased sensitization. The pathology results from the union of the antigen and the antibody.

There are thought to be two types of Rh antibodies: agglutinins and glutinins. The latter are smaller and pass through the placenta more readily. Therefore, when they are present in the maternal circulation early in pregnancy they also enter the fetal circulation early and react to the detriment of the fetus over a prolonged period. Hydrops foetalis may be produced. On the other hand, the agglutinins, when present, pass through to the fetus primarily through a damaged placenta—the trauma resulting from labor and delivery. The resultant terminal shower of antibodies may cause icterus gravis neonatorum or hemolytic anemia of the newborn.

Describe in detail the tuberculin test.

Tuberculins commonly used are: (*a*) *Old Tuberculin* (*O. T.*) prepared by growing tubercle bacilli on 5 per cent glycerin broth for 6 weeks, killing the bacilli by heat, separating the bacteria from the liquid, concentrating the liquid to one tenth of its volume by evaporation and filtering; new tuberculin.

(*b*) *Tuberculin residue, bacterial emulsion* (*T. R.* or *B. E.*) prepared by drying the bacilli over phosphorus pentoxide, grinding them to a powder, and suspending them in 50 per cent glycerin so that each cubic centimeter contains 5 mg. of bacterial substance.

(*c*) *Purified protein derivative.*

The *Mantoux test* is generally employed. It consists of the intracutaneous injection of 0.1 cc. of Old Tuberculin in 1:1000 dilution (0.1 mg. Old Tuberculin), or the use of two doses of purified protein derivative (*P.P.D. I* and *P.P.D. II*), the second dose being given 48 hours after the first dose, if the first dose is negative. A positive Mantoux reaction consists of an area of erythema and infiltration reaching its maximum in 48 hours following injection.

The *von Pirquet test* consists of the application of Old Tuberculin to a scarified area of skin; the *patch test* consists of the application of a piece of filter paper containing dried Old Tuberculin to the skin by means of adhesive.

Define mallein.

Mallein is a product obtained from cultures of the glanders bacillus in the same manner as Koch's original tuberculin. A 6 weeks' old culture, grown in 5 per cent nutrient glycerin-veal bouillon, is evaporated to one tenth its volume and the result is *mallein.* It is employed as a diagnostic agent in the same way as tuberculin.

Mention the laboratory procedures which aid in the diagnosis of viral infections; list several diseases in which each is specifically recommended.

(1) Cultivation or isolation in susceptible animal or embryonated eggs: herpangina, myalgia. (2) Serological diagnosis by (*a*) complement fixation: epidemic encephalitis, mumps, LGV; (*b*) hemagglutination-inhibition: influenza; (*c*) agglutination: primary atypical pneumonia; (*d*) direct microscopic examination: herpes simplex.

For the serologic diagnosis of virus diseases, what procedure should be followed in submitting specimens to the laboratory?

Two clotted blood specimens are preferred, one drawn during the acute phase of the disease, and another 10 to 14 days after onset (convalescent phase). This procedure is recommended for two reasons: (1) Antibody develops early in the course of certain diseases and may be present in low titer in the acute phase specimen; (2) the patient may have antibody in the blood before the onset of the disease, as a result of a previous clinical or subclinical attack or vaccination. By using two specimens, collected at the times indicated, it is usually possible in most cases of actual viral infection to demonstrate a sharp rise in antibody titer. In most instances, at least, a four-fold difference in titer between the acute and convalescent sera is considered diagnostic.

Mention the nature and value of coccidioidin, histoplasmin, blastomycin and sporotrichin in diagnosing mycotic infections.

These are type-specific vaccines that have been found valuable in demonstrating cutaneous hypersensitivity to *Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatitidis,* and

Sporotrichum schenkii. Inject 0.1 cc. vaccine intracutaneously. Reaction may be immediate or delayed for 24 to 48 hours and, occasionally, for as long as 2 weeks. A positive test is indicated by the occurrence of a wheal at least 1 cm. in diameter associated with erythema.

Name the laboratory procedures most helpful in assisting in the diagnosis of rickettsial disease.

(1) Complement fixation; (2) specific agglutination; (3) Weil-Felix test, using strains OX19, OX2 and OXK; (4) cultivation in embryonated eggs.

Section 6

MEDICINE

GENETICS AND DISEASE

Discuss the role of genetic factors as the cause of human disease.

Although there are conditions in which the genetic constitution is the major factor in determining the nature of the individual, in general there is an interaction between hereditary factors and the individual's environment that is important in the clinical manifestation of a disease. For example: (1) A particular disease or characteristic always occurs in those individuals who inherit the appropriate gene. In these individuals there is complete hereditary determination (blood groups, hemophilia, albinism, etc.). (2) A characteristic occurs in some individuals of a particular genetic constitution but does not express itself in others because they are not exposed to environmental influences that are necessary for the development of the trait (drug-induced hemolytic anemia, occurring in individuals whose erythrocytes have the inherited deficiency of glucose-6-phosphate dehydrogenase; these individuals show no evidence of disease unless they are exposed to certain drugs or other compounds). (3) A disease may occur in individuals of any genetic constitution with the same frequency and with no relation to the genetic constitution. Under these circumstances the condition is entirely determined by environment.

INFECTIOUS AND ALLERGIC DISEASES

How would you classify pneumonias?

With the advent of modern antimicrobial agents, the traditional classification into bronchial and lobar pneumonias became outmoded. It is more important to classify pneumonias according to the causative organisms. The more commonly encountered pneumonias include those produced by pneumococci, streptococci, staphylococci, klebsiellae, *H. influenzae,* and tubercle bacilli. Less frequently encountered pneumonias include those due to the bacillus of tularemia and to rickettsiae. Most of the viruses responsible for pneumonias are not known. Some are due to the psittacosis group. Allergic pneumonias (Loeffler's syndrome) and certain chemical fumes may cause pneumonia.

Differentiate typical pneumococcic lobar pneumonia from primary atypical pneumonia (viral).

Both diseases are usually preceded by an acute upper respiratory infection, but the severity of the chills, chest pain, and malaise that dramatically mark the onset of pneumococcic pneumonia often lead the patient with pneumococcic pneumonia to date the onset of his illness from these acute manifestations, whereas the patient with viral pneumonia will more often describe a gradual onset. The triad of chills, chest pain, and rusty or bloody sputum is more often present in pneumococcic pneumonia; any or all of these symptoms may be lacking in viral pneumonia. Physical examination more often demonstrates the classic signs of dyspnea, cyanosis, dullness, increased fremitus, and bronchial breathing with rales in pneumococcic pneumonia; but in both forms physical signs may be minimal and even absent. X-ray examination is not a reliable means of differentiating the two. Viral pneumonia may appear as lobar consolidation, and pneumococcic pneumonia is often patchy and scattered. Demonstration of pneumococci in the sputum is not proof of bacterial etiology; a considerable number of pneumococci are often found in the sputum of patients with viral pneumonia. The presence of a marked leukocytosis is strong evidence of a bacterial pneumonia. During or after an attack of viral pneumonia, the serums of the majority of patients contain increased titers of cold hemagglutinins or of agglutinins for streptococcus MG.

List the complications which may occur with pneumococcic and viral pneumonias.

Pneumococcic: Empyema, pleurisy with effusion, massive atelectasis, lung abscess, pericarditis, endocarditis, meningitis, arthritis.

Viral: Myocarditis, pseudobronchiectasis, and acute hemolytic anemia (especially in those with high titers of cold agglutinins).

Give treatment for staphylococcal pneumonia; why is the prognosis poor?

If the staphylococcus is sensitive to penicillin, 2,000,000 to 4,000,000 units of penicillin G should be administered intramuscularly in divided doses every 4 hours. If the organism is sensitive to erythromycin or chloramphenicol, one of these agents is added in a dose of 0.5 gm. orally, or intramuscularly, every 4 hours. If the staphylococcus is resistant to penicillin and is sensitive to vancomycin (Vancocin), the latter agent is administered 0.5 to 1.0 gm. intravenously every 12 hours. Recently, good results have been obtained in penicillin G resistant staphylococcal infections with methicillin (Celbenin, Staphcillin) 1 gm. every 4 to 6 hours parenterally. Ristocetin (Spontin) also represents an effective antistaphylococcic agent but must be administered intravenously. If intravenous therapy is impossible, kanamycin (Kantrex) 0.5 gm. intramuscularly every 8 hours is given. Regardless of which regimen is selected, it is important to continue treatment for at least 2 weeks. The disease is accompanied by a high mortality rate, largely because of the characteristic formation of many small abscesses throughout the lung parenchyma; also, this disease often represents a metastatic process from elsewhere in the body.

Differentiate between joint pains of subacute rheumatic fever and nonrheumatic "growing pains."

In rheumatic fever the symptoms occur most commonly between 6 and 8 years of age and often occur after an upper respiratory infection. The pains usually last all day, especially on motion, are localized in the joints of upper and lower extremities, and often are accompanied by slight increased local heat and mild swelling. In addition, these pains are often accompanied by other manifestations, such as nose bleeds, skin rash, pallor, fever, etc. A family history of rheumatic fever may be elicited. In nonrheumatic "growing pains," the symptoms may begin in early childhood and continue through adolescence, the pains being worse at the end of the day and during the night. The pain is most commonly in the muscles of legs and thighs, but occasionally involves the knee joints, and there is no local evidence of inflammation. As a rule, there are no other manifestations and a familial history of rheumatic fever is uncommon. The final differential rests on the laboratory findings (sedimentation rate, antistreptococcal titers, etc.).

Discuss relapses following an attack of scarlet fever.

Recovery from scarlet fever is usually associated with a permanent immunity to the rash toxin, and second attacks are rare. However, subsequent infections with a new serological type of hemolytic streptococci may occur and episodes of tonsillitis and pharyngitis occur frequently in persons who have had scarlet fever.

Outline the treatment for a case of subacute bacterial endocarditis in which the offending organism is not known.

In such instances, one must assume that the infection is caused by a resistant organism, such as enterococcus. Treatment consists of aqueous penicillin G intramuscularly, 1,000,000 units every 3 hours; streptomycin, 1 gm. intramuscularly every 12 hours; and Benemid, 0.5 gm. orally every 6 hours for 4 to 6 weeks; occasionally bacitracin is added. Anticoagulants should not be used. The sedimentation rate serves as a useful guide to the success of therapy.

Differentiate between meningococcic and pneumococcic meningitis.

Meningococcic meningitis is usually a primary disease with a sudden onset giving rise to signs of meningeal involvement within a few hours. Pneumococcic meningitis is usually associated with some other disease process, such as otitis media, mastoiditis, sinusitis, pneumonia, etc. Although it may have a sudden onset, there is usually evidence of sepsis for a longer period before meningeal symptoms develop. Bacteriological examination of spinal fluid usually gives the final answer.

Discuss the clinical picture and management of Waterhouse-Friderichsen syndrome in a case of meningococcemia.

Clinically, this syndrome represents one of sudden circulatory collapse, as a result of adrenal apoplexy giving rise to an adrenal crisis. Early symptoms include irritability, nausea, vomiting, abdominal pain, headache, and a high fever. Shortly after the onset, a petechial rash appears, which progresses rapidly to form a diffuse confluent purpuric eruption. Until recently, the disease was uniformly fatal, but, with the now available agents for the control of sepsis, adequate adrenal cortical hormone and cardiovascular supportive measures, instances of recovery are being reported with increasing frequency. However, it should be pointed out that meningococcemia with a purpuric rash may be associated with circulatory collapse without pathological evidence of acute adrenal cortical insufficiency. Blood eosinophile counts may be helpful in differentiating the two conditions. Usually an eosinophile count of 100 cells per cu. mm. is suggestive of adrenal cortical failure.

The treatment of Waterhouse-Friderichsen syndrome is one of providing adequate adrenal cortical hormone, control of sepsis, and support of the cardiovascular system: penicillin aqueous intramuscularly 500,000 units every 4 to 6 hours; continuous intravenous infusion of 5 per cent glucose in saline; 200 mg. of hydrocortisone (free alcohol) in 5 per cent glucose in a separate intravenous infusion; cortisone, 25 mg. intramuscularly or orally every 6 hours, with a gradual decrease in total daily dosage depending on the clinical course. In addition, Neo-Synephrine, 5 to 10 mg., may be added to the continuous infusion as necessary to maintain the blood pressure. Norepinephrine may be employed in the same manner.

What are the outstanding symptoms of brucellosis? Outline treatment for a case of acute brucellosis resulting from the ingestion of raw cow's milk.

Brucellosis may simulate a variety of infectious diseases, in that the symptomatology is a varied one. However, the most outstanding symptoms are those of weakness, sweating, and chilliness. The sweating usually occurs at night and the chilliness is noted most often when the patient is ambulatory. In mild cases, weakness is often the sole symptom.

The specific treatment of choice for acute brucellosis (*B. abortus*) is tetracycline, 500 mg. orally every 6 hours for 21 days, plus streptomycin, 1 gm. intramuscularly every 12 hours for the first 14 days of therapy. In critically ill patients, cortisone may be administered for the first 2 to 3 days. In cases of relapse, treatment should be repeated.

Define salmonellosis.

The term "salmonellosis" implies the infection of a human or animal by one or several of the more than 200 bacterial serotypes comprising the genus *Salmonella*. Included in this group are the organisms more familiarly known as the "typhoid-paratyphoid" bacilli. Thus, persons infected with either S. *typhosa* or S. *choleraesuis* are classified in each instance as having salmonellosis. A major difficulty in accepting the broad point of view stems from the older concept that infection with S. *typhosa* results in a serious septic disease, while infection with S. *paratyphi* A, B, or C is associated with less severe disease. However, greater familiarity with salmonellosis has resulted in the realization that any one of several clinical syndromes may be produced by the same or different salmonella serotypes. In view of the varied manifestations of salmonellosis, it has been suggested that signs and symptoms be classified into four clinical syndromes, which would facilitate arriving at a clinical diagnosis. These are as follows: gastroenterocolitis, seen in approximately 67 per cent of cases; septicemic or typhoidal syndrome, approximately 15 per cent; focal manifestations, approximately 8 per cent; or, an asymptomatic carrier state, approximately 10 per cent.

Outline the treatment for *Salmonella* gastroenterocolitis.

Treatment is largely symptomatic, in that the intestinal tract is freed naturally of a large number of salmonella organisms by diarrhea. Likewise, salmonellae ingested with contaminated food do not find conditions suitable for multiplication in the intestinal tract, since the normal microbial flora prevent this process, hence it is important not to interfere with the normal microbial flora by the administration of antimicrobics, especially the broad spectrum antibiotics. In those cases which are more severe, or prolonged, chloramphenicol, 0.5 gm. orally every 6 hours, may be tried. Certainly, protracted therapy should be discouraged, since the resultant disturbances in enteric flora may precipitate a generalized infection or produce an undesirable toxic effect.

Describe the clinical manifestations and treatment of salmonellosis due to *S. typhosa* (typhoid fever).

Clinical Manifestations: (1) Gastrointestinal: nausea, vomiting, diarrhea or constipation, abdominal pain and distention. (2) Nervous: headache, delirium, stiffness of neck, drowsiness, and stupor. (3) Pulmonary: productive cough and chest pain. (4) Urinary: frequency and dysuria. (5) Skin: "rose spots." (6) Sepsis: chills, fever, and prostration.

Treatment: (1) Good nursing care is vital. (2) Adequate soft or liquid diet with vitamin supplement. (3) Daily baths with alcohol rub. (4) Tepid sponge bath for temperature above 104°F. (5) Low enema preferable to purgatives. (6) Chloramphenicol 0.5 gm. orally every 6 hours for 14 consecutive days; or for 5 days, then omitted for 5 days and administered again for 5 days (the latter regimen is attended by fewer relapses). (7) Cortisone may be helpful in very toxic cases.

What organism is responsible for most cases of bacteriogenic "food poisoning"?

Enterotoxins liberated by staphylococci present in such food as Hollandaise sauce, chicken-a-la-king, custard pie, cream-filled eclairs, ham, and tongue.

List the various forms of and specific treatment for tularemia.

Ulceroglandular, typhoidal, pleuropulmonary, and ophthalmic.

Streptomycin intramuscularly 0.5 gm. every 6 to 8 hours for 5 to 6 days. In cases with large tularemic exudates the possibility of a Herxheimer reaction exists, which is a consequence of effective therapy and not an indication for more treatment.

What conditions influence the development of clinical tuberculosis?

(1) Diabetes, (2) silicosis, (3) tuberculin in large doses, (4) occupations in which there is exposure to tubercle bacilli, (5) trauma, and (6) allergy (sensitivity of the tissue to tuberculoprotein).

Give the three basic principles of therapy for pulmonary tuberculosis in order of their significance.

(1) *Systemic:* adequate nutrition and limitation of physical activity. (2) *Surgical:* correction of certain mechanical factors which prevent adequate control of the disease. (3) *Antituberculous agents.*

Outline the use of the antituberculous agents in pulmonary tuberculosis.

Streptomycin, isoniazid (INH) and paraaminosalicylic acid (PAS) are the principal drugs used in the treatment of tuberculosis. As a rule, two of the three drugs are administered simultaneously; as yet no combination has been demonstrated to be superior to another. However, streptomycin and isoniazid are considered the major drugs and are not usually administered simultaneously, but either one is used in combination with PAS. Thus, one major drug is withheld in case of drug toxicity or if resistant bacilli occur. Almost never is it permissible to give one antituberculous agent by itself. The usual doses are streptomycin, 1.0 gm. intramuscularly twice a week; isoniazid, 100 mg. 3 times a day by mouth; and PAS orally, 3 gm. 4 times daily. Duration of drug therapy is usually 12 to 18 months, depending on the length of time that elapses before stability of the disease is achieved. Other antituberculosis drugs that are sometimes helpful are viomycin, pyrazinamide (PZA), and cycloserine.

Give indications for surgical resection in pulmonary tuberculosis.

(1) The so-called "destroyed lung"; (2) residual cavities that persist after 6 months or more of antimicrobic therapy; (3) severe bronchial stenosis; (4) tuberculoma; (5) bronchiectasis associated with tuberculosis, and (6) "thickened pleura."

Describe the clinical features and treatment of sarcoidosis.

Sarcoidosis is a disseminated disease of unknown etiology, thought by some to represent an anergic form of tuberculosis. The characteristic lesion is a noncaseating tubercle. Most commonly involved are the lungs, mediastinal nodes, peripheral lymph nodes, corneal tract of the eye, the skin, the lacrimal and parotid glands, the tonsils and spleen. The heart, kidneys and gastrointestinal tract may be involved. In spite of extensive involvement patients show no toxemia, and symptoms are due only to mechanical effects. The tuberculin test is negative or slightly positive. Serum globulin is often elevated. Proof of *diagnosis* is obtained by biopsy of lymph node, skin lesion, or tonsils. Recovery occurs in many patients without treatment. To the present, most treatment has been of doubtful value and at best temporary in nature. Local injection of cortisone into the skin lesions may produce complete regression of the lesions injected. Likewise, oral therapy with cortisone has given promising results but the patients must be carefully selected, in view of the possibility of an exacerbation of tuberculosis and spread of sarcoidosis ("rebound relapse") after steroid therapy has been stopped. Cortisone is not recommended for asymptomatic patients, but rather for those disabled by respiratory or renal insufficiency, uveitis, parotitis, or myocardial involvement.

Define shigellosis (bacillary dysentery).

This is an infectious disease characterized by pyogenic inflammatory lesions of the large bowel. The causative agents of the disorder belong to the genus *Shigella;* the more important pathogens are: *Sh. dysenteriae, Sh. flexneri, Sh. boydii,* and *Sh. sonnei.* The cardinal clinical symptoms are diarrhea, tenesmus, and abdominal cramps.

Describe the symptoms of tuberculous meningitis.

The *onset is insidious* and is preceded by prodromal symptoms—peevishness, loss of appetite, fitful and broken sleep, headache, grinding of the teeth. The first stage, or *stage of irritation,* may be ushered in by a convulsion or the triad of headache, vomiting, and fever. *Headache* is intense; the child puts its hand to its head and from time to time gives a sudden cry—the so-called "hydrocephalic cry." *Vomiting* occurs without apparent cause and independently of taking food. *Fever* is moderate—102° to 103°F. Pulse is at first rapid, and later irregular and slow. The pupils are contracted. The bowels are obstinately constipated. The child is excited. During the *second stage* the irritative symptoms subside, and the child becomes dull and apathetic. Vomiting ceases; the abdomen is retracted or scaphoid; the head is thrown back; and muscular rigidity and convulsions occur. The pupils are dilated or irregular, and strabismus may develop. The *temperature* is variable, but not usually much elevated. The final stage, or *stage of paralysis,* is marked by increasing coma, convulsions, and spasms in various parts of the body. The pupils are dilated and the eyes only partially closed; the ocular muscles may be paralyzed. The pulse becomes rapid and feeble, and the patient sinks into the *typhoid state.* Sometimes an agonal rise of temperature takes place. A moderate leukocytosis (10,000 to 15,000) may be present throughout the course of the disease.

Discuss the role of lumbar puncture in patients suffering with purulent meningitis.

The primary purpose of a lumbar puncture is for diagnosis; only on rare occasions is it necessary to repeat it during therapy. In general, intrathecal therapy is not required and is often harmful.

What diseases are caused by (1) adenoviruses, (2) ECHO viruses, (3) Coxsackie viruses, and (4) respiratory syncytial viruses?

(1) *Adenoviruses* are a group of viruses that cause catarrhal inflammation of the pharynx and eye (pharyngoconjunctival fever). Pneumonia has been observed in association with this infection. The clinical characteristics of the disease are similar to those of primary atypical pneumonia, but significant increases in titer of cold hemagglutinins or of agglutinins for streptococcus MG do not occur.

(2) The *ECHO* (enteric cytopathogenic human orphan) viruses have been recognized as causing epidemics of diarrheal disease, as well as an aseptic meningitis without paralysis or sequelae.

(3) The *Coxsackie viruses* fall into two groups, A and B. Group A causes herpangina and possibly a nonfatal type of aseptic meningitis. Group B viruses

apparently cause epidemic pleurodynia (Bornholm disease).

(4) The *respiratory syncytial viruses* give rise to acute febrile respiratory illnesses, ranging from mild coryza to bronchitis, bronchiolitis, and bronchopneumonia.

Discuss the treatment and prognosis of infectious mononucleosis.

There is no specific treatment. Bed rest is indicated during the febrile stage and, if hepatitis is a complication, until it has subsided clinically and chemically. In severe cases, cortisone may be used, but only if covered with a wide-spectrum antibiotic. The prognosis is usually good, and the acute phase subsides within three weeks. Fatalities are due to rupture of the spleen or to respiratory paralysis associated with Guillain-Barré syndrome.

What are the complications and sequelae of pertussis (whooping cough)?

Bronchopneumonia is a frequent complication; pleurisy and lobar pneumonia sometimes occur. Petechial hemorrhages involving the face and the conjunctivae, epistaxis, and hemoptysis; convulsions; hemiplegia and monoplegia rarely occur. Sudden death may result from a subdural hemorrhage. Pulmonary tuberculosis not infrequently develops after whooping cough.

Define epidemic parotitis (mumps). What complications may arise in the course of this disease?

An acute contagious disease characterized by moderate constitutional symptoms and swelling and inflammation of the parotid and other salivary glands. The complications that may arise are swelling of the testicles, ovaries, and mammary glands. Pancreatitis and encephalitis occur less frequently and usually in adult patients.

Discuss the various factors concerned in the common cold.

Infections of the respiratory tract are encountered more often than any other groups of diseases in the practice of medicine, and the common cold is the chief offender. Almost everyone suffers with one or two attacks of this disease during the year and, although the common cold is not a serious illness per se, it nevertheless represents both a serious economic and a medical problem. From the economic standpoint, it is virtually impossible to estimate the annual cost of this disease. Common colds result in more lost time in working hours than any other single cause of disability, with financial loss both to the individual and to industry. In addition, untold sums of money are spent on medicines and methods of prevention, which have already proved valueless, such as vitamins, nose drops, gargles, vaccines, baths, sleeping porches, and wintering in warm climates. Medically, the common cold is important because of the diseases that arise from it (sinusitis, otitis media, bronchitis, pneumonia, etc.), or that may resemble colds in their early stages (streptococcic pharyngitis, scarlet fever, poliomyelitis, measles, pertussis, etc.).

List the prognostic factors in epidemic hemorrhagic fever (Manchurian fever).

No single finding is of great prognostic value in individual patients. However, prolonged high fever, protracted or recurrent shock, and persistent hemoconcentration are all ominous features. With rare exceptions, survivors who have not had central nervous system hemorrhages make complete recoveries. The case fatality rate is approximately 5 per cent.

What is the Stevens-Johnson syndrome?

This disease is characterized by a sudden onset with high fever, malaise, and ulcerative lesions of the conjunctivae, mouth, genitalia, and anus, followed in several days by a generalized bullous eruption. Although the etiology of this syndrome is unknown, a similar clinical picture has occurred following the use of sulfonamides, particularly sulfamethoxypyridine (Kynex, Medicil).

Define cat-scratch disease.

This is a self-limited type of granulomatous lymphadenitis, probably caused by a virus of the lymphogranuloma-psittacosis group and definitely associated with contact with cats. Fever is variable. A transient papule occurs at the site of entry and the regional lymph nodes become greatly swollen; then over a period of weeks or months the lesions slowly subside, with or without suppuration. The picture resembles that of lymphogranuloma venereum and a specific cutaneous test, comparable to the Frei test, is helpful in establishing the diagnosis.

Give the period of incubation and of eruption of the exanthemata.

INCUBATION

(a) *Scarlet fever:* A few hours to a week.
(b) *Measles:* About 2 weeks.
(c) *Rubella:* About 2 weeks.
(d) *Variola:* From 1 to 3 weeks.
(e) *Varicella:* One to 2 weeks.
(f) *Roseola infection:* About 5 days.

ERUPTION

(a) End of first or beginning of second day.
(b) On the fourth day.
(c) On the first or second day.
(d) On the third or fourth day.
(e) On the first day.
(f) Third to fifth day.

Give the symptoms of epidemic influenza.

The *onset* is sudden, with fever, headache, and pain in the back and limbs. The prostration is out of proportion to the fever, which is usually moderate, and the other constitutional symptoms. The headache is severe and obstinate, usually frontal.

Various types are distinguished. (*a*) *Respiratory:* The most common form is characterized by coryza and bronchitis. The fever is usually high, and the prostration and debility very great. Pneumonia, pleurisy and empyema may develop as complications. (*b*) *Gastrointestinal:* Onset is with nausea and vomiting, or abdominal pain and diarrhea. Duration and severity are very variable and relapses are common. Jaundice may occur and the spleen is often enlarged in the severer cases. Sudden onset with profuse diarrhea and little constitutional disturbance is sometimes observed. (*c*) *Nervous:* Catarrhal symptoms are not marked; there is severe headache, with pain in the back and joints and great prostration. Meningitis, brain abscess, and numerous disturbances of the nervous system may result from this form. (*d*) *Febrile:* Fever is the most prominent symptom. It may be remittent, with chills, or continued, and may simulate typhoid fever.

Give the etiology, symptoms and treatment of acute anterior epidemic poliomyelitis.

Etiology: The disease is due to one of the smallest filtrable viruses, which probably gains access to the central nervous system by way of the gastrointestinal tract. The disease is most likely spread by direct contact with infected human beings, carriers, or contaminated food. Flies may act as a reservoir of infection. Cases are observed chiefly in late summer or early fall. Most patients are under 15 years of age. Recent tonsillectomy predisposes to the disease, especially the bulbar form.

Symptoms: In moderately severe forms the *onset* is sudden, with fever up to 103°F., vomiting, restlessness, pain in the back and extremities, and symptoms of coryza or infection of the ears. Until the appearance of paralysis the symptoms are not distinctive. The *palsy*, which is flaccid, may come on within 24 hours of the onset, or be delayed 3 or 4 days. Individual groups of muscles, one or both legs, or the trunk or upper extremities may be involved. The paralysis rapidly reaches its maximum, but is quite variable in different muscle groups. In favorable cases, muscular power begins to return after a week or 10 days, and improvement continues until all but a small remnant of paralysis, usually in the legs, remains, which, however, is permanent. The blood shows *aleukocytosis.* The cerebrospinal fluid shows an increase of protein content and a *lymphocytosis* (up to 40 per cent). The *knee jerks* are early diminished and soon abolished altogether. Delirium is rare; the *sensorium* is unaffected. Constipation is more frequent than diarrhea.

In *abortive cases* so-called, the symptoms are very mild and there is no actual paralysis, although general muscular weakness and disinclination to use the limbs may be noted.

Other types are the *acute ascending*, the *bulbar*, and the *encephalic* forms. In the two former death sometimes occurs from respiratory paralysis.

Treatment: Most mild cases require no special treatment. In the acute stage the patient should be isolated, put to bed, and given good nursing care with relief of symptoms. Pain and muscle spasm may be relieved by hot applications or possibly by neostigmine (Prostigmin) and physostigmine. A paralyzed part should be protected but not fixed in a splint. Bulbar involvement may require suction or parenteral feeding. A respirator will be required for paralysis of respiratory muscles. In convalescence the patient should have orthopedic supervision.

Discuss the management of acute infectious hepatitis (virus A).

Regardless of the severity of an attack of this disease, the most important therapeutic measure is physical rest. Not infrequently, a mild case is converted into a severe one because of undue exercise. Likewise, relapses and retarded convalescence are often the result of too early ambulation. In general, complete bed rest is advised during the acute stages and, as the systemic symptoms subside, bathroom and chair privileges are allowed. The size and tenderness of the liver are followed closely, as well as changes in the liver-function tests. Ambulation is best prohibited until the liver returns to normal size and is no longer tender; also until a drop in blood bilirubin to 1.2 mg. or less and a retention of Bromsulphalein of less than 10 per cent after 45 minutes is obtained. Obviously, any untoward physical or chemical changes demand a return to bed rest. In addition, the diet should be high in protein and carbohydrate and low in fat. With an adequate diet, supplementary vitamins and certain lipotropic agents are not necessary, although there are some who advise them, especially the latter: methionine, choline, vitamin B_{12}, or crude liver extract. At times, sedation is necessary and, in such cases, chloral hydrate usually suffices. In severe cases, the administration of a wide spectrum antibiotic may be of some value in the control of organisms invading the liver area from the gastrointestinal tract. Finally, cortisone and ACTH may be tried in cases showing a downhill course, because they may help deposit glucose in the liver and delay liver degeneration.

What complications may occur with herpes zoster (shingles)?

Postherpetic neuralgia or paralysis, corneal ulceration with trigeminal herpes, encephalitis or myelitis, and secondary bacterial infection of rash.

Differentially diagnose chancre, chancroid, and herpes progenitalis.

CHANCRE	CHANCROID	HERPES
Origin: Due to inoculation with the discharges of the first and second stages of a syphilitic lesion.	Due to inoculation with the discharge of a chancroidal sore. Bacillus of Ducrey.	(1) Mechanical irritation, as in sexual intercourse. (2) Chemical irritation, such as is produced by acid discharges or by uncleanliness. (3) Often follows fever.
Incubation: From ten days to eight weeks. Average about three weeks.	No definite period. Usually two or three days.	None.

CHANCRE	CHANCROID	HERPES
Number: Single, at times simultaneously multiple.	Frequently multiple, often on opposing surfaces by auto-inoculation.	Multiple. Ultimately often confluent.
Beginning: Begins as an erosion, papule, tubercle, or ulcer. May remain without ulceration through its entire course.	Begins as a pustule or an ulcer. Always ulcerates.	Begins as a group of vesicles, which may coalesce or may ulcerate singly.
Depth: Usually superficial, saucer-shaped.	Hollow, excavated, or "punched out."	Superficial.
Secretion: Scanty serous, never auto-inoculable.	Abundant, purulent, readily auto-inoculable.	Moderate; several drops can be squeezed out. Usually does not auto-inoculate.
Induration: Almost always present, firm, parchment-like, sharply circumscribed.	Only exceptionally present. Is not sharply circumscribed.	Usually not present.
Sensibility: Very rarely painful.	Often painful.	Often painful.
Course: Progressively toward a cure, often healing spontaneously. Relapses and phagedena do not occur.	Irregular; may cicatrize rapidly or may extend. Relapses and phagedena not uncommon.	Easily and quickly cured. Sometimes spreads by the appearance of successive crops of vesicles; also recurs in unclean persons with long foreskins.
Inguinal adenitis: Constant, painless, multiple, generally bilateral; nodes usually do not break down.	Very frequent, painful, unilateral, inflammatory; an abscess is usually formed.	Very rare; when present, usually unilateral.
Prognosis: Good locally, usually does not leave a scar.	More serious locally, usually scars, at times becomes phagedenic.	Always good. Recurrences are frequent; leaves no scar.

Differentiate the early eruption of syphilis and measles.

SYPHILIS

History of chancre 6 weeks previous to eruption.
Fever usually absent; presence of mucous patches in oral cavity.
Eruption copper-colored and not especially prominent on face.

MEASLES

History of acute onset with fever and catarrhal symptoms 3 days before eruption appears.
Symptoms of coryza, conjunctivitis, and usually bronchitis with cough, Koplik spots.
Eruption appears first on face and rapidly spreads to entire body.

List the more common manifestations of congenital syphilis.

Interstitial keratitis, deafness, hutchinsonian teeth, hydarthrosis of the knees, osteomyelitis, and neurosyphilis.

What does the term "masking of syphilis" mean?

Not infrequently, gonorrhea and syphilis are contracted simultaneously and the administration of the dosage of penicillin required for the treatment of gonorrhea retards the development of the chancre and prolongs the incubation of syphilis.

What is the treatment of choice for primary and secondary syphilis?

Penicillin represents the best form of treatment for infective syphilis. In fact, penicillin is superior to all other forms of therapy in all types of syphilis. If penicillin is contraindicated, chloramphenicol or tetracycline may be employed.

What factors tend to influence the relapse rate in syphilis?

Age, sex, race, acquired immunity, treatment, stage of disease when treatment started, and resistance to treatment.

Is it advisable in the treatment of neurosyphilis to administer bismuth or mercury before giving penicillin to avoid a possible Herxheimer reaction?

No. It appears that such a danger following penicillin has been exaggerated.

What represents the most important single cause of death in endemic typhus fever?

The shocklike syndrome—peripheral circulatory failure, low blood pressure, hemoconcentration, and alteration in the blood chemistry and urine. No doubt, toxemia plays a role, but the generalized capillary inflammation undoubtedly is a contributory factor.

Differentiate clinically between endemic typhus and Rocky Mountain spotted fever.

Endemic typhus is usually seen in late fall and winter and is essentially an urban disease. Rocky Mountain spotted fever occurs in the spring and early summer and is usually a rural disease. The rash of endemic typhus appears first on the back and chest, later spreads to the abdomen and extremities, but usually spares the face, palms, and soles. In Rocky Mountain spotted fever the rash appears initially on the flexor surfaces of the wrists and ankles and back and then the forehead, arms, legs, chest, and abdomen, and still later on the palms, soles, and scalp. Not infrequently, the mucosae of the mouth and vagina show the eruption.

What is the chief clinical manifestation of psittacosis (ornithosis)?

Interstitial pneumonitis varying in severity from mild to fatal.

Give the clinical picture of an untreated case of lymphogranuloma venereum (lymphopathia venereum, climatic bubo).

The initial vesicle occurs at site of invasion, 5 to 14 days after exposure. After the vesicle bursts, a granulomatous chancre forms, usually on the glans penis, vagina, cervix, or labia. The second stage consists of invasion of lymphatic nodes with buboes in inguinal region (males) and in the retroperitoneal, retropelvic, and perianal regions (female). This stage is often associated with signs of sepsis. In the third stage, one finds elephantiasis of the genitalia, perirectal abscesses, fistulae, and stricture of the rectum.

Describe the clinical features of coccidioidomycosis.

Infection occurs by inhalation of the spores of *Coccidioides immitis*, and in this country occurs only in the endemic desert areas of the Southwestern states. Erythema nodosum occurs in almost 10 per cent of those infected. Although symptoms may be few, x-ray examination will often show an acute pneumonia. After resolution of the pneumonia there may persist one or more nodules or thin-walled cavities, which simulate tuberculosis and neoplasms. In a small percentage of cases a fatal disseminated form occurs, with widespread osseous involvement. *Diagnosis* may be established by culture of the sputum or gastric washings, by use of the coccidioidin skin test, and, in the primary phase, by serological reaction. In most cases complete recovery occurs. Persistent primary lesions may be resected. For the rare granulomatous phase, the only internal medication of any real promise is amphotericin B (Fungizone).

Discuss the symptomatology of toxoplasmosis.

The symptoms vary with the location of the parasites in the body. In the acute form there is high fever, a macular skin eruption, mental stupor, and atypical pneumonia. Chronic encephalitis symptoms such as convulsions, hemiplegia, mental deterioration, and excessive nervousness may occur.

Discuss the problems concerned with the treatment of histoplasmosis.

The specific effectiveness of antibiotic and chemical agents in the treatment of this disease is difficult to evaluate in that the clinical manifestations are protean as a result of several factors—namely, the biological properties of the fungus, the type of infection, the distribution and size of lesions, the immune status of the patient, and the histological features of the lesions. In a number of instances the disease is benign and the patient shows no signs of illness. In others, a massive inoculum and/or a poor resistance of the host leads to death. For chronic cavitary and disseminated histoplasmosis, amphotericin B (Fungizone) is the treatment of choice. However, in considering the use of chemotherapeutic agents in histoplasmosis one must consider the possibility that the drug may antagonize or counteract one or more of the several mechanisms that are significant in a patient's natural resistance.

Define and give treatment for actinomycosis.

A slowly progressive chronic disease characterized by a granulomatous type of inflammatory reaction and abscess formation with multiple draining sinuses, from which typical "granules" are discharged. Treatment consists of procaine penicillin intramuscularly, 1,000,000 to 3,000,000 units daily for 10 days. Sulfadiazine orally is given at the same time, beginning with 1 gm. every 6 hours until clinical improvement is manifested and 1 gm. daily thereafter for an indefinite period (1 to 3 months). In addition, the patient should receive a saturated solution of potassium iodide, initial dose of 3 drops 3 times daily, the dose increased by 3 drops each day up to 30 drops 3 times a day. Finally, all accessible lesions should receive roentgen irradiation.

Give two types of nocardiosis.

(1) A chronic suppurative infection of the subcutaneous tissues and bones that results in tumefactions or mycetoma. (2) A systemic infection, usually pulmonary in origin, that results in widespread multiple metastatic abscesses.

List the dangers of parasitic infestations.

(1) Worms may injure organs mechanically. Hookworms can damage the intestinal wall and cause bleeding; blood flukes are injurious to capillaries, etc. They may obstruct ducts—liver flukes in bile ducts, filariae in lymphatics. (2) The host may absorb toxic substances produced by the parasite. (3) Trauma caused by the worm may provide a portal of entry for other organisms, especially bacteria. (4) The worms may deprive the host of food.

Give the symptoms related to the three periods of development in trichinosis.

During the first period, nausea, vomiting, and diarrhea which lasts about one week, as a result of the acute inflammation and hemorrhage of the upper small intestine. The second stage is one of myositis involving chiefly the diaphragm and muscles of the arms, legs, intercostals, larynx, and mouth. Dyspnea and edema often occur during this period. The third stage is the critical one, with edema and cachexia, and in serious cases delirium, profound dyspnea, and coma.

List the complications of bacillary dysentery.

Arthritis, hepatitis, neuritis, parotitis, uveitis, and stenosis of colon.

Give the symptomatology and complications of amebiasis.

The symptoms vary from those of slight disturbance of the intestinal tract to those of severe dysentery. Liver abscess occurs in approximately 15 per cent of cases. Abscess of the brain, spleen, and other viscera, and appendicitis may also develop as a result of this disease.

Discuss the clinical manifestations and treatment of moniliasis (*Candida albicans* infection).

The clinical manifestations of moniliasis have been known for many years. Oral thrush, usually a mild infection, may become a more serious condition, especially in debilitated children and in the elderly (particularly diabetics), by extension to the pharynx, bronchi, or esophagus and may reach the kidneys, brain, and other organs. The largest percentage of cases are those involving the skin, but the gastrointestinal and vaginal forms are common. Within recent years, with the widespread use of the antimicrobial agents there has been a considerable increase in the incidence and severity of *Candida* infections. However, the mere finding of the fungus in the sputum, stool, etc., does not establish it as the cause of the pathological condition, as *C. albicans* is a frequent secondary invader.

For localized skin and intraoral lesions, gentian violet (1 per cent aqueous solution) applied twice daily is usually effective. For cases of vaginitis, good results often follow the local use of nystatin (Mycostatin) vaginal tablets (100,000 units) instilled twice daily for a week. Likewise, nystatin oral tablets (500,000 units) 3 times daily by mouth are often beneficial in treating intestinal moniliasis. However, for the hematogenous, pulmonary, and meningeal types, all forms of therapy are for the most part disappointing. Because nystatin is poorly absorbed through the gastrointestinal tract amphotericin B (Fungizone) is the drug of choice at the present time.

Discuss the chemotherapy of malaria.

In general, the chemotherapy of malaria may be considered under the following categories:

(*1*) *True Causal Prophylaxis:* chloroguanide (Paludrine). At this time an ideal causal prophylactic agent is not available. However, chloroguanide (Paludrine) does exert an effect against falciparum parasites and, to a lesser extent, against vivax infections.

(*2*) *Suppressive Treatment:* Although infection is not prevented by suppressive treatment, the erythrocytic stage of development of the parasites is inhibited so that the subjective clinical manifestations do not occur. Chloroquine (Aralen) and chloroguanide (Paludrine) represent the two most effective drugs for suppressive treatment.

(*3*) *Control of Clinical Attack:* Chloroquine (Aralen), chloroguanide (Paludrine), and amodiaquine (Miaquin, Camoquin) are the drugs of choice in interrupting the erythrocytic schizogony of the malarial parasite and thus terminating the clinical attack.

(*4*) *Radical Cure:* The eradication of both erythrocytic and exoerythrocytic parasites of an established infection in a patient who has left a hyperendemic malarious area is best obtained in vivax malaria with primaquine alone or in combination with quinine or chloroquine (Aralen), or the combination of chloroquine (Aralen) and pamaquine (Plasmochin, Aminoquin). For cure of falciparum malaria, the continuation of suppressive therapy is sufficient.

Outline the management of the inflammatory stage of dermatophytosis (athlete's foot, trichophytosis).

Treatment consists of bed rest and the application of wet dressings. At first, continuous wet dressings of Burow's solution (aluminum acetate diluted 1:15), boric acid solution (4 per cent), or potassium permanganate (1:10,000 dilution). As the acute process subsides, the compresses are applied at increasingly greater intervals. After the inflammatory process is minimal, the wet dressings are discontinued and lotions (calamine), pastes (Lassar's) and paints (Castellani's) are used in the order named. In addition, local surgical measures (opening of blebs and vesicles) will hasten recovery. As a rule if the infection is due to fungi other than *T. rubrum,* topical therapy alone will prove adequate. If *T. rubrum* is causing the infection, oral griseofulvin (Fulvicin, Grifulvin, Griseo-Fulvin) should be added.

Outline the causes of allergy.

In general, the causes of allergy may be divided into two groups: (1) *predisposing causes,* as an inherited predisposition or exposure to allergenic substances adequate to stimulate antibody response, and (2) *exciting causes* which include extrinsic allergens (inhalants, ingestants, injectants, and contactants) and intrinsic agents, particularly bacteria. In addition, such factors as emotional disturbances, temperature extremes, sunlight, etc., may induce allergy.

Of what value are elimination diets and provocative feedings?

Although skin testing may furnish valuable clues in searching for offending allergens, the ultimate test depends on clinical trial. This can be done by eliminating all foods from the diet to which any suspicion is attached. If, after 7 days, the symptoms are relieved, one may assume that one or more of the eliminated foods are at fault. The patient is then given large quantities of one of these foods at each meal and, usually, if it is responsible for the disease, symptoms develop within 12 to 48 hours. The same procedure is carried out with all suspicious foods.

Define asthma and name four types.

Asthma is a specific type of dyspnea (gasping) produced by generalized narrowing of the bronchiolar lumina. (1) *Allergic* asthma, resulting from allergen-antibody reactions in the bronchial wall; (2) *infectious* asthma, associated with infections of the respiratory tract; (3) *cardiac* asthma, in patients with left heart failure, giving rise to bronchiolar edema, and (4) *psychogenic* asthma, the exact mechanism of which is not fully understood.

What are autoimmune diseases?

The autoimmune diseases are a group formerly regarded as unrelated but now closely associated because much evidence suggests that they all have the same basic immunological mechanism. Each is thought to be caused by the development of antibodies to cells in some part of the body. The pathological and clinical picture produced depends on what bodily tissues are attacked by autoantibodies and thus may vary during the course of the disease, which often is quite chronic. The basic mechanism leading to the development of such a disorder has been claimed to be an alteration in the composition of normal body protein, thus rendering it antigenic. Factors causing this change may be invasion of cells by bacteria or viruses or union of cells with drugs thus forming protein conjugates that lead to the formation of autoantibodies. Examples of diseases thought to be caused by autoimmune processes include, among others, acute rheumatic fever, rheumatoid arthritis, systemic lupus erythematosus, certain demyelinizing diseases, idiopathic thrombocytopenic and drug-induced purpuras, thyroiditis, and acquired hemolytic anemia.

Give the treatment for infective asthma.

(1) Appropriate antimicrobial therapy during acute stage. (2) Adequate drainage of involved paranasal sinuses, with local measures and, if indicated, surgical attack. (3) Autogenous bacterial vaccines. (4) Chemoprophylaxis during fall and winter months if recurrences are frequent.

Differentiate between urticaria, eczema, and angioneurotic edema.

Urticaria: This type of skin allergy is characterized by wheals or welts (hives), which erupt on any part of the body. They usually itch intensely, persist for a variable time, and then disappear entirely, leaving no trace.

Eczema (atopic or neurodermatitis): Although any part of the body may be involved, the flexures overlying joints are the most frequent sites. The skin lesions may be dry or weeping, raw or crusted, depending on the intensity of the reaction. The itching is almost always very marked.

Angioneurotic Edema: Characterized by subcutaneous swelling of the skin and mucous membranes; frequently accompanied by itching, burning, or prickling sensations; may involve any portion of the body surface or of the mucous membrane. Involvement of certain areas, e.g., edema of glottis, may prove fatal.

Discuss the clinical manifestations of stings of five hymenoptera that occasionally cause death.

The venom of the wasp, yellow jacket, hornet, honeybee, or bumblebee, when injected into man, produces allergic sensitization. Manifestations vary from local intense burning with rapid pulse, sense of suffocation, and cough to vasomotor rhinitis, asthma and general edema, blurred vision, vascular collapse, loss of sphincter control, and unconsciousness. The symptoms seem to become more severe with each episode of stinging. In fatal cases, autopsy observations include general visceral congestion with petechial hemorrhages, myocarditis, and edema of the larynx.

Outline treatment of status asthmaticus.

Treatment is directed toward relieving bronchial obstruction caused by edema of the bronchial mucous membranes, secondary to increased capillary dilatation and permeability, spasm of the smooth muscle wall, and hypersecretion of the bronchial mucous glands. The following measures are carried out: (1) Patient should be hospitalized in that it removes from him possible allergens in his own environment. (2) Intermittent oxygen therapy. (3) Bronchial dilator drugs: (*a*) epinephrine administered subcutaneously (dilution 1:1000) 0.3 to 5.0 cc. every 4 hours as necessary, intramascularly (peanut oil 1:500) 0.5 to 1 cc. every 12 hours, or by inhalation (dilution 1:100) every 2 to 4 hours if necessary; (*b*) ephedrine 25 mg. subcutaneously every fourth hour, beginning two hours after starting epinephrine. (4) Bronchoscopy to remove mucus plugs may be life-saving, especially in bronchial stenosis. (5) Aminophylline is often helpful and is best administered very slowly, intravenously 0.5 gm. once or twice daily. (6) Potassium iodide (saturated solution), 10 to 15 drops by mouth, 3 or 4 times daily, has proved valuable in reducing the viscosity of the bronchial secretions. (7) Fluids, orally or parenterally, are essential in that dehydration is often present. (8) Opiates are *never* used in the treatment of asthma (abolishment of cough reflex and reduction in respiratory rate). Sleep is important in asthmatics, as they are apprehensive, etc., and this is best achieved with chloral hydrate 0.5 to 1 gm. orally or by rectum. (9) Steroid therapy: ACTH, cortisone, hydrocortisone, and more recently prednisone and prednisolone have all been successfully employed in this disease. ACTH is the preparation of choice and is given intravenously (20 units in 1,000 cc. of 5 per cent glucose in distilled water by slow drip for 8 hours) and repeated every 8 hours during the first 24 hours if the condition warrants. As improvement occurs, one may proceed with ACTH gel (40 units intramuscularly daily), which is then tapered off gradually, depending on the course of the disease. Although ACTH is usually helpful, at times it is necessary to resort to one of the other preparations: hydrocortisone intravenously (100 mg.) daily for 2 to 3 days; if the desired effect is obtained, one can change to oral administration (200 mg.) daily in 3 divided doses for 2 days, 100 mg. daily for 2 days, and finally 60 mg. daily in 2 divided doses, after which the dose is gradually tapered off.

Give the symptoms associated with acute systemic lupus erythematosus (SLE).

(1) Fever, usually irregular, with a tendency to remissions; (2) involvement of the synovial and serous membranes (polyarthritis, pleuritis, pericarditis); (3) depression of bone-marrow function (leukopenia, hypochromic anemia, thrombopenia); and (4) vascular alterations in the skin, retina, kidneys, and other viscera.

Discuss the diagnosis and treatment of polyarteritis (periarteritis nodosa).

Because of the nature of this disease, it may simulate a great many other disorders. The diagnosis depends on a positive biopsy (skin, subcutaneous tissue, or muscle). For the most part, treatment is disappointing, in that, despite healing of the arterial lesions, the interference to blood flow in various vital organs is so great that death occurs. At present, ACTH and the cortisone group of drugs are the best form of therapy, because with their use, especially in early cases, remissions can often be induced, although upon cessation of therapy, the disease usually relapses. An occasional case of periarteritis will recover spontaneously.

What is the significance of erythema nodosum?

This type of rash usually results from allergic reactions to various infective agents and certain drugs. It occurs most frequently as a sequela of hemolytic streptococcic diseases but may be associated with tuberculosis, ulcerative colitis, coccidioidomycosis, lymphopathia venereum, sarcoidosis, and other systemic diseases. The drugs most frequently causing this type of reaction are the sulfonamides, thiouracil, bromides, and iodides. Because of the possible implications of serious systemic diseases, careful diagnostic studies to establish the cause are warranted in all cases.

Describe the pulmonary and esophageal manifestations of progressive systemic sclerosis (scleroderma).

Cyanosis and dyspnea as a result of a diffusion fibrosis of the lungs; difficulty in swallowing as a result of atrophy and sclerosis of the esophagus; and later, nausea, vomiting, and pain because of a partial obstruction with the development of a chronic esophagitis.

DISEASES OF THE RESPIRATORY SYSTEM

Define chronic laryngitis.

For all practical purposes, it is well to assume that there is no such disease until it has been proved by histopathological studies of tissues removed at laryngoscopy. Persistent hoarseness of several weeks may be due to neoplasm, syphilis, or tuberculosis.

Discuss the value of bronchoscopy in diagnosis and treatment.

Diagnostic bronchoscopy is indicated whenever bronchial disease is suggested by persistent wheeze, physical signs of atelectasis or localized emphysema, when x-ray examination suggests pulmonary neoplasm, when pneumonias fail to undergo resolution, and whenever other diagnostic methods fail to establish the diagnosis of a pulmonary disease. It is also indicated whenever there is a question of foreign body, bronchiectasis, lung abscess, or benign or malignant neoplasms of the lung. All patients with pulmonary tuberculosis should have bronchoscopy before a decision is made concerning the use of collapse therapy. Bronchoscopy may be of value not only for obtaining biopsies but for providing aspirated material for bacteriological and mycological examinations.

Bronchoscopy is of *therapeutic* value in the removal of foreign bodies and for the removal of aspirated material that may have produced atelectasis. Some cases of bronchial adenoma may be treated bronchoscopically.

Name the most common causes of hemoptysis.

(1) Pulmonary tuberculosis.
(2) Bronchiectasis.
(3) Bronchogenic carcinoma.
(4) Bronchial adenoma.
(5) Mitral stenosis.
(6) Pulmonary infarct.
(7) Pneumonia.
(8) Blood dyscrasias.
(9) Overdosage with anticoagulants.

Differentiate hemoptysis and hematemesis.

HEMOPTYSIS

(1) Often preceded by cough or signs of pulmonary or cardiac disease.
(2) Blood coughed up; vomiting, if it occurs, follows the cough.
(3) Blood frothy, bright red, and alkaline; mucopus may be mixed with it.
(4) Cough persists, with signs of local disease in chest; sputa continue to be blood stained.

HEMATEMESIS

(1) Previous history of gastric, hepatic, or splenic disease.
(2) Blood vomited.
(3) Blood dark, usually clotted, mixed with food and acid.
(4) The hemorrhage is followed by tarry stools, and signs of abdominal disease may be detected.

What is the treatment of pulmonary hemorrhage?

Morphine is *contraindicated,* since its suppression of the cough reflex results in "trapping" of the blood with resultant bronchial obstruction and atelectasis. Barbiturates and small doses of codeine may be used to relieve the patient's apprehension. If the bleeding is believed to come from the upper lobes, the patient should be kept in a semisitting position. Pulmonary hemorrhages are rarely if ever due to hematological or chemical deficiencies, and the use of coagulants, calcium, etc., is of no value. Pulmonary bleeding very rarely goes on to exsanguination, and measures such as the induction of pneumothorax are rarely justifiable.

Give causes of hemothorax.

Perforating wounds, fracture of ribs, rupture of an aneurysm into the pleural sac.

Distinguish pleural effusion, pneumothorax and atelectasis by physical examination.

Pleural Effusion: Inspection and palpation may reveal enlargement of the affected side, bulging of interspaces and diminished motion, and diminished tactile fremitus. The trachea and the heart are displaced to the contralateral side. The percussion note is usually dull or flat, and breath sounds are distant or absent.

Pneumothorax: Inspection and palpation may reveal enlargement of the affected side if a tension pneumothorax is present. Tactile fremitus is diminished or absent. The trachea and heart may be displaced to the contralateral side. The percussion note is characteristically hyperresonant. Breath sounds are distant or absent.

Atelectasis: Inspection and palpation may reveal retraction of the affected side and diminished motion, and the trachea and heart may be found to be displaced toward the affected side. Tactile fremitus may be decreased or increased. The percussion note may be dull or flat. Breath sounds may be diminished or absent, but under certain conditions bronchovesicular or bronchial sounds may be audible.

List the causes of hemorrhagic pleural fluid.

Tuberculosis, neoplasm involving pleura, thoracic trauma, spontaneous hemopneumothorax, pulmonary infarction, and acute pancreatitis with peritonitis.

Describe the management of pleurisy with effusion.

Diagnostic thoracentesis at least once is indicated. In examination of the fluid, special attention should be given to determine the cell count and the differential count. Either the specific gravity or the protein content should be determined. The fluid should be cultured for pyogenic organisms as well as on special media for tubercle bacilli. Guinea-pig inoculation is valuable. Smear examination rarely demonstrates tubercle bacilli. Cytological examination for neoplastic cells should be made.

If bacteriological proof of the etiology is not obtained and if the effusion cannot be attributed to cardiac or to neoplastic disease, the effusion should be considered to be of tuberculous origin. Sterile effusions are very rarely due to pneumonias. Since one third of patients with so-called "idiopathic" pleurisy usually develop tuberculosis unless treatment is taken, all such patients should receive a period of 6 months' rest in a sanatorium or its equivalent at home. Aspiration of fluid or induction of pneumothorax has not been found of value. Periodic x-ray examinations should be made for 3 years after the effusion. *Intercostal procaine infiltration* should be used in preference to adhesive strapping if pain is severe.

Differentiate chronic bronchitis and bronchiectasis.

The characteristic history in both diseases is chronic cough with or without expectoration, hemoptysis, and especially a history of recurrent attacks of pneumonitis which may have been variously diagnosed as pneumonia, pleurisy, grippe, etc. Profuse or foul expectoration is encountered only in advanced cases of bronchiectasis. Physical examination may reveal scattered, dry, moist, or sibilant rales in the case of chronic bronchitis. Signs of atelectasis or of localized rales of any variety may be present in bronchiectasis, but in both conditions physical examination may be negative except for signs of emphysema. The chest x-ray may appear normal in both diseases. A *bronchogram* is essential to differentiate chronic bronchitis from bronchiectasis. Valuable confirmatory evidence may be obtained by bronchoscopy.

What is the treatment of bronchiectasis?

Bronchiectasis is best treated by *lobar resection*. If extensive bilateral bronchiectasis is present, resection of segments of the lobe may permit bilateral surgical removal of diseased lung tissue. Ordinarily it is not justifiable to attempt surgical removal in a case of bronchiectasis unless complete removal of the diseased tissue is feasible and allows an adequate amount of lung tissue to remain.

The *medical treatment* of bronchiectasis includes intensive treatment of the usually associated sinusitis, postural drainage for patients who have expectoration, measures directed toward improvement of nutrition, and the prevention or prompt treatment of acute respiratory infections. Prompt treatment of minor upper respiratory infections by bed rest and appropriate antimicrobial therapy will usually be effective in preventing the attacks of pneumonitis to which patients with bronchiectasis are prone. Repeated bronchoscopic aspiration is rarely indicated. Removal to a milder and dryer climate produces a great improvement in some cases but is disappointing in many instances.

Describe the etiology of spontaneous pneumothorax and outline the management.

Spontaneous pneumothorax is associated with pulmonary tuberculosis in only 5 per cent of the cases. The remainder are believed to be due either to rupture of a superficial pulmonary bleb or to a *pleural tear* secondary to spontaneous pneumomediastinum. The clinical detection of the characteristic precordial click will indicate that in a given case the pneumothorax is secondary to mediastinal emphysema.

Treatment consists of bed rest only so long as dyspnea or pain persists. Aspiration of air should be done only for relief of severe dyspnea and in most cases is not necessary. If the lung fails to reexpand gradually, the presence of a bronchopleural fistula should be suspected. Thoracoscopy and even thoracotomy may be indicated in rare instances.

Outline the treatment of primary lung abscess.

Antimicrobials have revolutionized the treatment of this disease. The most effective agent is determined by sensitivity studies. Drainage of the abscess is to be avoided if possible because drainage alone seldom cures the lesion and a persistent bronchocutaneous sinus is established. However, a patient who is toxic, continues to run a high temperature, and has an abscess with copious sputum, despite specific antimicrobial therapy, requires surgical drainage.

What is the significance of calcified pulmonary nodules?

Pulmonary calcifications were until recently considered to be due to healed childhood tuberculous lesions. Recently, however, it has been demonstrated that a considerable proportion of pulmonary calcifications are due to healed lesions of *histoplasmosis*. Infection with this fungus is most common in Missouri and surrounding states. Calcification in a person with a negative tuberculin test and a positive histoplasmin test may be considered due to histoplasmosis, and vice versa. If both skin tests are positive it may be impossible to determine the etiology. The calcifications due to histoplasmosis have no clinical significance.

Calcifications due to childhood tuberculosis are likewise without significance in the vast majority of cases; very rarely a calcified tuberculous lesion may result in progressive pulmonary or miliary tuberculosis.

How would you diagnose carcinoma of the lungs?

The development of cough, hemoptysis, or chest pain in a male more than forty years of age should lead to a consideration of carcinoma of the lung. If carcinoma of the lung is to be detected in an operable stage, the diagnosis must be made within a short time after the onset of symptoms. Dyspnea and weight loss are usually symptoms of advanced inoperable carcinoma. Physical findings in the lungs may be negative except for a localized wheeze in the early stages. Later, emaciation and signs of atelectasis and effusion will be found. X-ray examination and bronchoscopy with examination of biopsy tissue, cytological study (Papanicolaou type) of aspirated bronchial secretion and pleural fluid and node biopsy are the most useful methods of establishing the diagnosis. Exploratory thoracotomy should be employed if symptoms and x-ray findings persist even though bronchoscopic examination is negative.

List the symptoms of and treatment for middle lobe syndrome.

The right middle lobe is particularly vulnerable to atelectasis. The symptoms are commonly chronic cough, with or without productive sputum, and recurrent attacks of pneumonitis with fever and hemoptysis. The proper treatment is extirpation of the diseased lobe.

Discuss the symptomatology of emphysema.

The earliest and most prominent symptom is dyspnea on exertion, which is progressive and is aggravated by respiratory infection, altitude, and high humidity. An early morning cough, which is relatively nonproductive, and weakness, weight loss, ankle edema, and wheezing are indicative of this condition.

Describe the principal postoperative pulmonary complications.

(1) The onset of cough, dyspnea, chest pain, and fever within 48 hours of operation is usually due to *massive atelectasis.* Physical examination will reveal the mediastinal shift and suppressed breath sounds. X-ray examination will give more definite evidence. Bronchoscopy is both diagnostic and therapeutic.

(2) Chest pain or hemoptysis occurring 5 to 14 days after operation is most commonly due to *pulmonary infarction.* Chest examination may reveal tenderness on local pressure. A few rales may be audible. X-ray examination may be negative, or it may reveal pulmonary densities simulating pneumonia, a small effusion or merely elevation of the diaphragm. Evidence of *thrombosis* in the deep calf veins should be sought by eliciting pain in the calf on dorsiflexion of the foot (*Homan's sign*) or tenderness on firm compression of the calf muscles against the tibia (*Moses' sign*). Venous thrombosis may not become manifest until several days later.

(3) *Bacterial* or *viral pneumonia* may occur after operation but is much less common than pulmonary infarction.

(4) Infarcts and areas of *atelectasis* may undergo necrotic changes with the formation of *lung abscess.*

(5) Pulmonary *tuberculosis* may first be recognized as the result of respiratory symptoms developing after operation.

What is the treatment of pulmonary embolism?

Massive pulmonary embolism is usually preceded by one or more pulmonary infarctions or by evidence of venous thrombosis in the lower extremities. Antiembolic therapy should be immediately instituted as soon as either of these manifestations is recognized.

Medical therapy may comprise oral *Dicumarol,* parenteral *heparin* injections, or a combination of the two, in which heparin is administered during the first 24 to 48 hours, until Dicumarol becomes effective. Surgical therapy consists in early ligation of the involved vessels.

List the most common causes of acute mediastinitis.

This disease is always secondary to a primary infection elsewhere or to perforation of the esophagus or tracheobronchial tree.

What complicating diseases may occur with a diaphragmatic hernia?

Esophagitis, gastritis, or ulceration, as a result of reflux of gastric contents, sliding motion of the hernia, or constriction from diaphragmatic spasm.

How would you diagnose a pulmonary arteriovenous fistula or hemangioma?

Its presence should be suspected in patients with chronic cyanosis, without cardiac murmurs or enlargement to indicate the presence of cardiac anomalies. X-ray examination may reveal a density near the hilum on one or both sides. Angiography may be useful in demonstrating the hemangioma. Lobectomy may be curative.

What are the most common complications of acute barbiturate poisoning?

Atelectasis and pneumonia, as a result of decreased pulmonary ventilation and aspiration of vomitus.

Give the principal manifestations of berylliosis (beryllium poisoning).

Acute pneumonitis, chronic pulmonary granulomatosis, and contact lesions, such as dermatitis, subcutaneous granuloma, conjunctivitis, and corneal ulcer.

Define silo-filler's disease.

This syndrome is recognized among farmers who work with corn silage inside silos and is manifested chiefly by a severe form of pneumonitis. Apparently, the offending cause is a brownish or yellowish gas liberated by the silage; the quantity of gas given off is a product of the varying concentration of nitrate nitrogen in the corn itself and the vigor of the fermentative process. The properties of the gas are not unlike those of nitrogen dioxide and the clinical picture associated with the inhalation of nitrogen dioxide seems to parallel in many cases those seen in this disease. Whether this condition is in any way related to the syndrome of farmer's lung (pulmonary fibrosis) is at this time considered unlikely.

DISEASES OF THE DIGESTIVE SYSTEM

What are the most common causes of diseases involving the oral cavity?

(1) *Nutritional disturbances:* malnutrition giving rise to certain vitamin deficiency states, pernicious anemia, Plummer-Vinson syndrome, etc. (2) *Infectious diseases:* measles, scarlet fever, chickenpox, syphilis, tuberculosis, etc. (3) *Neoplasms.* (4) *Noxious substances:* bismuth, lead, Dilantin, mercury, arsenic, antimicrobial agents, etc.

Discuss the role of teeth in disease.

Mastication and the number, occlusion, and condition of the teeth are important to the health. Caries, lack of teeth, and poorly fitting dental plates interfere with mastication, with resulting loss of appetite, weight loss, and malnutrition.

What are the cause and significance of leukoplakia?

Leukoplakia results from such irritants as tobacco, alcohol, betel nut, and dentures. Since the condition may be precancerous, it should be treated promptly. In the early stages, avoidance of irritants often proves sufficient. In the latter stages, excision or cautery is indicated.

Discuss the etiology of xerostomia.

Xerostomia (dryness of the mouth) is caused by any state of dehydration, local infection of the salivary glands, salivary-duct calculi, or systemic diseases involving the salivary glands (Boeck's sarcoid [uveoparotid syndrome], Mikulicz's disease, etc.), or neurosis.

What condition may cause bleeding gums?

Bleeding gums are the result of engorgement and ulceration of the gingival tissue as a result of pyorrhea, chronic irritation from mechanical causes such as ill-fitting dentures and secondary infection, blood dyscrasias (leukemia, purpura hemorrhagica, aplastic anemia, etc.), scurvy, metallic poisonings (mercury, bismuth, and arsenic), and infection (Vincent's angina, etc.).

Give a classification of diseases of the esophagus.

(1) *Disturbances of motor function* (rapid ingestion of food, excessive smoking, emotional disturbances, focal neurological diseases, and so-called cardiospasm, the cause of which is unknown). (2) *Developmental abnormalities* (atresia, webs, diverticula, short esophagus, and paraesophageal hernia). (3) *Extraluminal disease* (mediastinal tumors and enlarged glands, aortic aneurysm, cardiac enlargement, pericardial effusion, etc.). (4) *Intraluminal disease* (inflammation, ulceration, perforation from caustics and foreign bodies, systemic infections, peptic ulceration superimposed on a developmental abnormality [especially a short esophagus], hiatus hernia, scleroderma, and certain granulomatous diseases such as syphilis and tuberculosis). (5) *Degenerative diseases* (deficiency states, such as pellagra and Plummer-Vinson syndrome). (6) *Neoplasms* (most frequently carcinoma of the lower and midportions of the esophagus).

What are the etiology, symptomatology, and treatment of esophageal varices?

Esophageal varices occur as part of the vascular congestive phenomena of portal obstruction resulting from cirrhosis of the liver (or congestive splenomegaly). This condition is asymptomatic, unless hemorrhage occurs as manifested by hematemesis and/or melena. Aside from the immediate problem of blood loss, therapy is directed to the underlying condition. Varices have been successfully injected with sclerosing solutions through the esophagoscope, but the procedure is dangerous and at best is usually only palliative. Tamponade by inflatable rubber bag has been recommended, with or without instillation of Gelfoam or similar coagulant. For intractable bleeding, transthoracic ligation of the varices may prove an immediate life-saving measure. Splenorenal anastomosis or portacaval shunt operations may be helpful in preventing future bleeding.

Differentiate between gastric ulcer and carcinoma.

(*1*) *Age:* Ulcer is seen most commonly between 20 and 50 years, whereas carcinoma is rare before 40.

(*2*) *History:* A long history of several years' duration, with periodic attacks, suggests ulcer, whereas a short history often occurs with carcinoma and periodicity is rare. Loss of appetite is much more common in carcinoma.

(*3*) *Laboratory:* The continual presence of occult blood in the stool after several weeks of therapy is suggestive of carcinoma, whereas a continued absence of occult blood suggests ulcer. Likewise, a progressive anemia more often accompanies a carcinoma. The demonstration of histamine achlorhydria rules out ulcer, but high acid values after histamine are seen at times with carcinoma.

(*4*) *Roentgenological and Gastroscopic Interpretations:* Both are of great differential value but not infallible.

(*5*) *Therapeutic Trial:* At times, the above criteria fail to give a definitive answer, and a short trial of medical treatment may be indicated in certain cases. In patients with a stomach secreting acid juice, the failure to obtain relief of pain or gain in weight, the continuance of occult blood in the stool, and absence of a rapid decrease in size of crater by roentgenological and gastroscopic examinations would surely indicate the diagnosis of carcinoma, and surgery should be carried out.

Outline the management of uncomplicated peptic ulcer.

The basis of treatment for uncomplicated peptic ulcer is rest and neutralization of acid.

Rest: Complete bed rest for a minimum of 2 weeks, preferably in a hospital, relaxation, avoidance of nervous tension, and diversion of nervous energy into some form of hobby, etc. As a rule, superficial psychotherapy and reassurance prove sufficient, but in certain cases formal psychiatric care may be necessary.

Neutralization of Acid: This is maintained by means of the acid-combining power of food proteins and by the acid-neutralizing capacity of various types of alkali. (*a*) The customary diet consists in the administration of 90 cc. of milk or milk and cream (equal amounts) every hour from 7 a.m. to 7 p.m. The second day, small additional feedings of soft food are begun, starting with one and increasing each day until the seventh day, when feedings are taken every 2 hours from 8 a.m. to 6 p.m. As a rule, the patient can resume a 3-meal regimen after 2 weeks. Food during the night is indicated only if pain appears. (*b*) Antacids (aluminum hydroxide, magnesium oxide or trisilicate, or calcium carbonate) should be given with or between the feedings of milk and cream and should be continued at bedtime. In some patients, milk, cream, and alkali should be continued throughout the night, or a continuous drip may be used. On occasion, gastric aspiration may be necessary, especially at bedtime; this not only decreases the period during which the ulcer is exposed to the action of the acid gastric content, but also affords valuable evidence regarding the rate of gastric emptying. (*c*) Medication: General sedation with phenobarbital is often desirable. In addition, efforts to lessen gastric secretion and motility are worthy of trial. Belladonna or atropine seem to be effective empirically. Likewise, one of the anticholinergic substances may be employed, such as methantheline bromide (Banthine) 50 to 100 mg. by mouth every six hours.

The above regimen is followed for 3 to 4 weeks, after which each patient is given instructions as to further care of his ulcer. Emphasis is placed on the fact that it is during the first 6 months that one has the opportunity to prevent chronicity (see next question).

What measures are employed to prevent ulcer recurrences?

Although the etiology of peptic ulcer is not known, there can be no doubt that aggravating factors are well recognized and in many instances can be avoided. (1) The fundamental principle of management is absolute regularity of diet, with frequent simple feedings, eaten slowly in a relaxed manner. The excessive use of alcohol, coffee, tea, or caffeine-containing drinks should be prohibited. However, in some instances the infrequent use of these stimulants is permitted on the basis of emotional factors. The same reasoning applies to the use of tobacco. (2) The factor of emotional stress and strain undoubtedly plays an important role, and the patient must be helped to prevent undesirable situations. An understanding physician can usually do more in this respect than a psychiatrist. (3) Intercurrent infection may precipitate the recurrence of an ulcer. Although no particular measures can be taken to control this threat, if infection does occur, the patient should be treated as if the ulcer were active. Furthermore, the infection should not be treated with antimicrobial agents likely to produce local gastric irritation such as chloramphenicol, tetracyclines, and sulfonamides, nor should salicylates be used to control pain. In this connection, the therapeutic use of the corticosteroids and butazolidine are contraindicated in any patient in whom an ulcer is suspected or is known to have previously occurred.

Give the symptoms and differential diagnosis of regional enteritis (terminal ileitis, Crohn's disease).

(1) The symptoms of this disease are varied. At times, the onset is acute and simulates acute appendicitis, and the diagnosis is revealed at operation. Frequently, there is a history of recurrent episodes of periumbilical or right lower quadrant cramps with diarrhea, slight elevation of temperature, occasionally nausea and vomiting, and a slight elevation in leukocytes, and the stools may show occult blood. There are usually right lower quadrant tenderness, some muscle rigidity, and a palpable mass in the region of the cecum. In chronic cases there are loss of appetite, diarrhea, and abdominal pain, which result in weight loss and nutritional disturbances.

(2) The differential diagnosis includes ulcerative colitis, tuberculosis enteritis, new growth, and, in acute cases, acute appendicitis. In regional enteritis there is no evidence of ulceration on sigmoidoscopy, although mucopurulent or bloody discharges may be noted coming down from higher up. Roentgen study of the colon and small bowel frequently shows a characteristic narrowing of the terminal ileum ("string sign"), or permanent deformity and irregularity of the normal patterns. When the disease is widespread, "skip areas" are seen at higher levels with or without areas of obstruction. In the absence of other evidences of tuberculosis, the diagnosis is usually one of regional enteritis.

Define malabsorption syndrome.

This term is used to include both primary and secondary sprue. Primary sprue is due to an inherent defect of the small intestine and takes the form of celiac disease in children and tropical or nontropical sprue (idiopathic steatorrhea) in adults. Secondary sprue may occur after surgery, particularly gastrectomy and resection or exclusion of a segment of small intestine. Gastrocolic or enterocolic fistulas and involvement of the intestinal wall by regional enteritis, Hodgkin's disease, or Whipple's disease may be responsible for secondary impairment of absorption. Malabsorption secondary to deficient digestive enzymes occurs as a result of chronic pancreatitis and complete obstruction of the common bile duct. Steatorrhea or the presence of excess fat in the feces is the characteristic feature of the malabsorption syndrome.

Discuss the etiology, clinical manifestations and treatment of pseudomembranous enterocolitis and staphylococcal enteritis.

Reports concerning pseudomembranous enterocolitis and staphylococcal enteritis complicating antibiotic therapy are appearing with increasing frequency. It has been pointed out that, although there is much resemblance in their clinical manifestations, pseudomembranous enterocolitis and staphylococcal enteritis apparently are two separate and distinct entities. The relationship between pseudomembranous enterocolitis, antibiotic therapy, and antibiotic-resistant staphylococci is probably not causal but coincidental. In staphylococcal enteritis the enteric mucosa remains intact, whereas in pseudomembranous enterocolitis the mucosa is denuded. In staphylococcal enteritis the early administration of an antibiotic effective against the staphylococci found in the stool usually leads to recovery. Such therapy is usually ineffective in pseudomembranous enterocolitis.

The pathogenesis of pseudomembranous enterocolitis is not clear. It usually follows operations on the bowel, but it has been seen in patients with bowel lesions who had not undergone operation or who had an entirely different type of illness. It is conceivable, in this antibiotic era, that some of these patients may also show resistant staphylococci in the stool. The presence of these organisms in large numbers may aggravate the underlying pseudomembranous enterocolitis.

Staphylococcal enteritis is a different pathological entity. It appears that the victims of this complication either harbor or contract from carriers staphylococci that are resistant to the administered antibiotic agent. These organisms then invade the intestinal tract, where an opposing normal flora has already been substantially suppressed by antibiotic therapy. In the intestinal tract the staphylococci grow in pure culture and most probably produce a toxin that causes the gastrointestinal and systemic symptoms—namely, azotemia. Not all of these symptoms are necessarily present in every case. In overwhelming toxemia the patient may die in a few hours, even before the onset of diarrhea. Staphylococcal enteritis has followed the administration of various antibiotics. It has occurred in both surgical and nonsurgical patients and in patients who received the drug orally or parenterally.

This entity may be treated successfully if (*a*) it is recognized early, (*b*) the offending antibiotic is immediately withdrawn, (*c*) this is replaced by erythromycin, and (*d*) the necessary supportive therapy (to maintain or restore fluid and electrolyte balance, blood pressure, etc.) is instituted. Erythromycin or novobiocin is generally recommended as the antibiotic of choice in this situation. However, sensitivity of the isolated pathogen should always be determined because of the possibility of resistant staphylococcal strains. Diarrhea during a course of antibiotic therapy is not always due to resistant staphylococci. The mild diarrhea without systemic reaction that so commonly arises during oral administration of the so-called broad-spectrum antibiotics is probably produced by chemical irritation, sensitivity to the drug, or disturbed intestinal milieu. Possibly in some such cases one may find an abundance of antibiotic-resistant staphylococci in the stool. Mild diarrhea without systemic symptoms will respond to the discontinuance of the offending antibiotic medication without any further measures.

List the common disturbances of the colon.

(1) Motor and secretory disturbances: "mucous colitis" or "irritable colon," atony of the bowel, constipation, and diarrhea. (2) Congenital abnormalities: megacolon (Hirschsprung's disease), diverticulosis. (3) Tumors: benign (adenomas, lipomas), malignant (carcinoma, sarcoma). (4) Inflammatory disease: due to infectious agents (*Salmonella,* agents of bacillary dysentery, amebiasis, etc.), ulcerative colitis of undetermined cause.

Differentiate between cerebral vomiting and gastric vomiting.

In *cerebral vomiting* the contents of the stomach are suddenly and violently expelled without cause, pain, or retching, and without reference to the taking of food; the pulse is slow and full. *Gastric vomiting* is preceded by nausea and epigastric pain and tenderness, and there are symptoms of some gastrointestinal disorder; the pulse is apt to be hurried and feeble.

What is the value of peritoneoscopy?

Peritoneoscopy is of value as a diagnostic aid in cases of ascites of undetermined origin. The procedure may provide visual or biopsy evidence of tuberculosis, carcinomatosis, or hepatic disease. In some quarters it is considered to afford a safer means to obtain liver biopsies than needle puncture. In other quarters exploratory laparotomy is preferred as a method of investigation in cases of ascites of unknown etiology.

Differentiate intestinal colic, uterine colic, and renal colic.

Intestinal Colic: The pain is diffuse or referred to the unbilical region and very severe, doubling the patient up. It is relieved by pressure and by the free discharge of flatus. The attack, as a rule, comes on suddenly and does not last long, and there is a definite history of some dietetic indiscretion.

Uterine Colic: The pain is localized in the pelvis and has somewhat of an intermittent, contractile character. There is usually a history of some uterine disorder.

Renal Colic: The pain begins in the lumbar region and shoots down the ureter to the side of the penis or labium. The testicle on the painful side is retracted. The attack is often accompanied by nausea, vomiting, and profuse sweating, and is relieved by the passage of gravel or calculi.

What is Virchow's node or signal node?

A lymph node or nodes located behind the middle third of the left clavicle at the junction of the lymphatic duct with the subclavian vein. It is a common location for metastatic lesions arising from the upper gastrointestinal tract.

Discuss the management of chronic ulcerative colitis.

For the most part, the management of this disease of unknown etiology is one of nonspecific and empirical measures, with surgery in certain cases. The effectiveness of medical therapy depends largely on the severity of the disease, which is determined by the number and character of the stools, the presence or absence of constitutional symptoms, erythema nodosum, arthralgia, and radiological and proctoscopic findings. In addition, certain factors affecting the course of the disease will influence the end results of therapy, namely, left-sided involvement only, mild beginning, and clinical recovery between attacks. These will respond to medical treatment, in contrast to those cases with an acute fulminating onset, right-sided disease, universal involvement, and continuous symptoms without remission in which unsatisfactory results are obtained.

Mild colitis is characterized by a mild diarrhea, with or without blood, and no constitutional symptoms; proctoscopic examination reveals finely granular mucosae with pin-point ulcerations; and a frequently negative radiological study may show tiny mucosal serrations; if the disease is of long standing, a narrow rigid colon may be present. Therapy for this type of colitis, which is often effective, consists of bed rest, a low-residue bland diet supplemented with vitamins, a poorly absorbable sulfonamide such as phthalylsulfathiazole (Sulfathalidine) 1 gm. 4 times daily; sedation; antispasmodics; Kaomagma 1 tablespoon 3 times a day; and psychotherapy in the form of encouragement, reassurance, and optimism.

The *moderately severe or severe cases* have marked diarrhea containing blood and mucus; fever; arthralgia; erythema nodosum; varying degrees of disability; an acutely inflamed, ulcerated mucosa covered with blood; and radiological evidence of ulceration. For this type, medical therapy offers about an even chance of being helpful. Treatment is best carried out in the hospital. In addition to the measures as outlined for the mild cases, the moderately severe or severe case should receive intravenous feedings of glucose, electrolytes, and vitamins as needed; liver extract, iron, and blood transfusions for anemia; penicillin intramuscularly (300,000 units) and streptomycin 0.5 gm. every 12 hours; and, finally, ACTH, which is often followed within 24 to 48 hours with marked clinical improvement. ACTH (20 units) is given intravenously in the glucose infusion over 18 hours for the first week and then gradually tapered off. After discontinuance of ACTH, the patient is maintained on cortisone as necessary.

The *fulminating type of colitis,* which is characterized by accentuation and rapid progression of all manifestations of the severe case, should receive the same medical regimen, but only as a preparation for surgery. Likewise, the moderately severe or severe cases which develop uncontrollable hemorrhage, perforations, obstructions, fistulas, or malignancies or fail to respond to medical treatment should have surgery, preferably a simultaneous ileostomy and colectomy.

Differentiate diverticulitis and carcinoma of the sigmoid.

Both conditions occur chiefly in older age groups and are manifested by constipation or obstruction and by rectal bleeding. Abdominal pain is more common in diverticulitis, while weight loss is more likely to occur with carcinoma. X-ray examination will usually succeed in differentiating the two conditions, but may fail to do so if the lesion is below the sigmoid. However, sigmoidoscopic examination is of value in visualizing such lesions and also permits biopsy. Cancer may develop in a diverticulum; and diverticulitis and cancer may coexist.

How would you make a diagnosis of tuberculous peritonitis?

Tuberculous peritonitis may occur as part of an acute generalized tuberculosis but often occurs without clinical evidence of tuberculosis elsewhere. Symptoms may develop acutely with high fever and abdominal pain or insidiously with slight fever, weight loss, anorexia, and abdominal distention. Ascites is usually present, but the effusion may be small and difficult to demonstrate. A characteristic "doughy" sensation may be obtained on abdominal palpation. The occurrence of such symptoms and signs in persons with evidence of pulmonary or genitourinary tuberculosis, or with possible salpingitis, or even the mere history of contact with tuberculosis will justify the clinical diagnosis of tuberculous peritonitis. Proof of the diagnosis can be obtained only by laparotomy or peritoneoscopy. A therapeutic test of streptomycin is justifiable at times.

Name five extra-abdominal diseases which may simulate an acute surgical abdomen.

(1) Basal pneumonias.
(2) Acute myocardial infarction.
(3) Tabetic crises.
(4) Lead colic.
(5) Crises of sickle-cell anemia.

Differentiate between diabetic acidosis and appendicitis.

(1) Vomiting precedes the onset of pain in acidosis and follows pain in appendicitis. (2) Pain is relieved upon control of acidosis, but persists if due to appendicitis. (3) Fever may or may not be present with either condition. (4) Leukocytosis is usually high in both, from either dehydration in acidosis or inflammatory changes in appendicitis.

Give the etiology and management of constipation.

In general, constipation is the result of (1) some organic cause: an abnormal systemic state (dehydration, hypothyroidism, deficiency disease, etc.); muscular weakness of the abdominal wall, pelvic floor, or intestinal wall (pregnancy, ascites, etc.), central nervous system disorders (spinal-cord disease, insanity, etc.); colon disorders (congenital defects, strictures, diverticulitis, external pressure by ovarian cysts, etc.); and many others; (2) bad habits: eating at irregular times, a diet consisting of concentrated food with little bulk, failure to respond regularly when the reflex for defecation is initiated, the frequent use of laxatives and enemas, and the belief that everyone should have a bowel evacuation every day.

The treatment of constipation depends largely on whether it is due to some organic cause or to bad habits. A thorough investigation to establish an organic cause is therefore important. For the management of simple constipation, the patient is instructed in good living habits—regulation of schedule so that adequate time is allowed for the development of a regular bowel-habit time, diet consisting of an adequate supply of essential foods (milk, eggs, meat, vegetables, fruits, butter and whole-grain cereals), and adequate fluid intake (at least 7 glasses daily). For the most part, the use of laxatives and enemas is not necessary and should be condemned. Older persons may require laxatives (aromatic fluid extract of cascara, 20 drops, or milk of magnesia, 1 to 2 teaspoons). Since mineral oil may interfere with absorption of fat-soluble vitamins and also may interfere with the normal dilating action of the stool, it is not recommended for regular use. For patients with severe constipation, it may become necessary in the beginning of the anticonstipation program to employ small oil-retention enemas at intervals. In addition, substances that supply artificial bulk are often helpful. Preparations derived from tragacanth (Saraka, gum karaya, Mucara, etc.), psyllium seed (Serutan, Siblin, Konsyl, Metamucil, etc.), and methyl cellulose (Cellothyl, Syrup Hydrolose, etc.) may be used in decreasing amounts as a regular bowel-habit pattern becomes established.

What is the significance of a "rectal shelf"?

When the rectovesical or rectouterine pouches are involved by metastasis, digital rectal examination will reveal a rectal shelf, sometimes called "Blumer's shelf." It is frequently encountered with primary carcinoma of the stomach.

Give a classification of diseases of the liver.

Acute Diseases: (*a*) Chemicals: chloroform, arsenic, cinchophen, carbon tetrachloride, phosphorus, trichlorethylene, etc. (*b*) Infections: virus (A and B) hepatitis, infectious mononucleosis, salmonellosis, yellow fever, spirochetosis icterohemorrhagica, parasitic infestations, especially amebiasis. (*c*) Acute biliary obstruction: Biliary calculi, new growth, postoperative trauma to the common duct, or the presence on the common duct of enlarged nodes due to infectious diseases, metastatic malignancy, or a generalized process such as Hodgkin's disease.

Chronic Diseases (chronic hepatitis, cirrhosis): For practical purposes, the fibrosis that is characteristic of chronic liver disease resulting from repeated insults or continuation of the various factors causing liver damage, namely, toxic agents, infections, progressive degenerative disease, prolonged partial biliary obstruction, vascular disturbance, etc. (*a*) Postatrophic cirrhosis, chronic viral hepatitis. (*b*) Laennec's cirrhosis (portal cirrhosis, alcoholic cirrhosis), probably due largely to a nutritional deficiency. (*c*) Biliary cirrhosis resulting from partial obstruction and infection of the large bile ducts. (*d*) Syphilitic cirrhosis (hepar lobatum), a manifestation of late acquired syphilis, resulting from a gummatous involvement of the liver. (*e*) Cardiac cirrhosis, always associated with chronic congestive heart failure.

Define "Charcot's intermittent hepatic fever."

Fever associated with an enlarged tender liver, jaundice, and chills is characteristic of a common-duct stone with cholangitis. Multiple cholangitic liver abscesses may be present.

Give the etiology and treatment of biliary dyskinesia.

This type of biliary colic is due to a disturbance in the reciprocal relationship between the gallbladder and the sphincter of Oddi, rather than to calculi or exudate. Contraction of the gallbladder normally results in relaxation of the sphincter of Oddi, but, if it does not relax, intrabiliary pressure increases with resultant colicky pain. This condition is characteristically relieved by nitroglycerine under the tongue.

What is "syringe" jaundice?

A type of infectious (virus B) hepatitis (homologous serum jaundice) resulting from the use of inadequately sterilized syringes (after injection of insulin, penicillin, etc.) that have been contaminated with serum or blood from a carrier of the virus, as well as by the administration of convalescent sera, plasma, or blood taken from persons who are carriers of the virus.

Differentiate between epidemic infectious (virus A) jaundice and homologous serum jaundice (virus B).

	EPIDEMIC INFECTIOUS JAUNDICE	HOMOLOGOUS SERUM JAUNDICE
Incubation period	Usually 7 to 30 days.	Usually 80 to 100 days.
Fever	Prominent.	Commonly lacking in pre-icteric stage.
Nausea and vomiting	Often severe.	Usually not severe.
Associated diseases (shigellosis, salmonellosis)	Often.	Uncommon.
History	Contact with cases.	Injections, transfusions, etc.

Give the clinical significance of carotinemia.

This condition is due to the ingestion of carrots, squash, spinach, oranges, egg yolk, and other sources of dietary pigment resulting in a xanthosis of the skin and increased lipochromes in the blood. Since pigmentation tends to parallel total serum lipids, the presence of carotinemia may denote hypothyroidism or diabetes, but usually the condition is harmless.

Of what value is Courvoisier's "law"?

The finding of a distended normal gallbladder in a jaundiced patient is pathognomonic of cancerous biliary obstruction, in that, in jaundice due to a common-duct stone, the gallbladder is usually atrophic or shrunken as a result of earlier inflammation and scarring, giving rise to thickening and inelasticity.

Outline the management of cirrhosis of the liver.

Rest: Patients with jaundice or intercurrent infection should be in bed; others should obtain sufficient rest.

Diet: This is the most important feature. It should consist of at least 3,000 calories (carbohydrate 300 gm., protein 125 gm., fat 140 gm.). If the patient eats poorly or is vomiting, protein hydrolysates orally or intravenously (along with 5 per cent dextrose solution) should be administered. Alcohol is forbidden.

Medication: Brewer's yeast, 30 gm. daily; multiple vitamins, one capsule or tablet 3 times a day; vitamin K (Synkamin) 4.8 mg. every third day; lipotropic substances such as choline or methionine may be used; iron in the presence of hypochromic anemia; B_{12} or liver extract if the anemia is macrocytic and/or peripheral neuritis is noted.

Ascites: If mild, this will usually respond to medical treatment. Paracentesis of the abdomen should be postponed as long as possible, since much protein can be wasted by repeated paracenteses. Mercurial diuretics and a low sodium intake are often beneficial, but the possibility of a resulting low salt syndrome must be kept in mind. Recently, the employment of cation exchange resins, which reduce the absorption of sodium from the intestinal tract, has made it possible to allow the patient more salt, which improves the palatability of the diet. However, when using a resin, one should make certain that acidosis and hypopotassemia do not occur. For the management of bleeding esophageal varices, see page 253.

Describe methods of lowering blood ammonia in hepatic coma.

(1) The protein intake should be reduced to zero for several days and then gradually increased as the patient becomes lucid; (2) oral bacterial suppressive agents, preferably neomycin (3 to 6 gm. daily) to reduce the contribution of nitrogen compounds from colon bacteria; and, (3) intravenous sodium glutamate (25 to 100 gm. daily) is believed by some to lower blood ammonia by the formation of glutamine. Likewise, intravenous L-arginine (25 to 50 gm. daily) is said to lower blood ammonia by furthering urea production.

What is the Cruveilhier-Baumgarten syndrome?

Development of a large umbilical or paraumbilical vein, producing a loud abdominal murmur and thrill, as the result of portal hypertension. Most instances are secondary to cirrhosis of the liver; very rarely, the result of congenital anomaly or absence of the portal vein.

What is the treatment for silent gallstones?

Patients with unsuspected cholelithiasis should have a cholecystectomy, unless there is definite contraindication, because (1) carcinoma of the gallbladder usually occurs in association with longstanding cholelithiasis, (2) the longer cholelithiasis exists the greater is the incidence of common-duct stone, (3) cholelithiasis may cause acute cholecystitis, and (4) its presence is associated with liver injury.

What is the relative frequency of carcinoma in ascending, transverse, descending and sigmoid portions of the colon, and in the rectum?

Cecum, 4.2 per cent; ascending colon, 3.7 per cent; hepatic flexure, 2.3 per cent; transverse colon, 4.1 per cent; splenic flexure, 2.8 per cent; descending colon, 3.4 per cent; sigmoid, 17.1 per cent; rectosigmoid, 10.6 per cent; rectum and anus, 49.9 per cent.

What is the value of liver biopsy? How may it be obtained?

Liver biopsy is of considerable value in the investigation of liver disease.

In jaundice, to differentiate between parenchymal disease and extrahepatic obstruction, when other tests are equivocal.

To follow the progress of hepatitis. This is particularly useful in the "post-hepatitis" syndrome for differentiating chronic or residual hepatitis from malingering.

To evaluate the results of therapy. The diminution of fatty infiltration is easily demonstrated by serial biopsies.

In suspected primary or metastatic neoplasm of the liver. If a primary lesion is known to be present elsewhere in the body, its management may be influenced by establishing the presence of hepatic metastasis. If no primary lesion has been found, a positive biopsy report may render surgical exploration needless.

For the definite diagnosis of hepatic cirrhosis and of systemic disease—hemochromatosis, lymphoblastoma, miliary tuberculosis, sarcoidosis, brucellosis, infectious mononucleosis, typhoid fever, amyloidosis, and von Gierke's disease.

Biopsies may be obtained in the enlarged liver by insertion of an aspiration needle or trocar below the costal margin. Especially when the liver is not prominently enlarged, the biopsy may be more safely obtained by peritoneoscopy or laparotomy.

Give the differential diagnosis of acute cholecystitis.

Ulcer is often difficult to distinguish from acute cholecystitis, especially after perforation has occurred. The history of gallstone colic, jaundice, and the location and character of pain are often helpful. A survey film of the abdomen, showing free gas in the peritoneal cavity suggests perforation by an ulcer. Right pyelonephritis can usually be ruled out by loin tenderness, plus the urinary symptoms and findings. Acute appendicitis in the early stage, before the pain has become localized, may at times prove difficult to differentiate.

What is mucoviscidosis?

This is the descriptive term applied to fibrocystic disease of the pancreas in childhood, the etiology of which is unknown. It is characterized by functional disturbances in the external secretory mechanism of the pancreas and in the mucous glands of the gastrointestinal and respiratory tract, and also of the sweat and salivary glands. Clinically, it is manifested by malnutrition, steatorrhea, chronic respiratory infections, and a deficiency in pancreatic secretions, particularly trypsin. A "sweat test" showing chlorides of more than 60 mEq./L. is diagnostic. In general, therapy has been unsuccessful, although the use of antimicrobial agents is helpful in combating infection, and the correction of sodium depletion as a result of salt loss through the skin has also improved the prognosis.

Differentiate abscess of the liver and cancer of the liver.

In *abscess* the history contains a definite cause—some acute infectious disease or disease of the gastrointestinal tract, tropical dysentery, etc. The enlargement is uniform and smooth and usually is attended with pain. The temperature is of the septic type, and there are hectic symptoms, sweats, etc. On aspiration, pus may be obtained. *Cancer* is a disease of middle life and is more often secondary to cancer in some other organ than primary. The surface of the liver is nodular, the enlargement is usually painless, and there is marked cachexia.

Define and give treatment for the "dumping" syndrome.

After a total, and sometimes after a subtotal, gastric resection, the reservoir function of the stomach having been removed, the ingested food may enter the jejunum rapidly, giving rise to a symptom complex called the "dumping" syndrome. The definite cause of this condition is unknown, but it may be due to (1) dilatation and irritation of the jejunum, (2) rapid changes in blood-sugar level, (3) vagal-sympathetic imbalance. The symptoms include one or more of the following: weakness, sweating, dizziness, nausea, vomiting, abdominal cramps or epigastric pain, diarrhea, and palpitation. Usually, the symptoms are mild and disappear within several weeks after the operation, but in some patients they are severe, with an occasional collapse, and will persist in varying degrees of intensity for months or even years. In the latter group, there is weight loss, anemia, or a spruelike syndrome. Treatment consists of a high protein–low carbohydrate diet, frequent small feedings, and little or no fluid with meals. Atropine is given to the point of tolerance.

What are the causes of deficiency diseases?

An insufficient intake, faulty absorption, impaired utilization or excessive loss of any of the nutriments, namely, proteins, vitamins, minerals, or inadequate caloric intake.

Discuss the development of undernutrition.

The term "undernutrition" refers primarily to a deficiency of calories and protein, although there may be a deficiency of other nutriments as well. For practical purposes, undernutrition is usually a mixed deficiency, in that a caloric deficiency disease becomes in effect one of protein deficiency. In the former, the protein is burned for fuel and thus there is an insufficient supply of protein for the body's needs.

List the common causes and clinical manifestations of a deficiency in sodium.

Diseases of the gastrointestinal tract (vomiting, diarrhea), pyelonephritis, diabetes mellitus, adrenal insufficiency, excessive loss of body fluids (draining sinuses, undue sweating, burns), use of low sodium diets, and mercurial diuretics. Sodium deficiency may result in electrolyte imbalance, oliguria, acidosis, anuria, and death.

Give the clinical and electrocardiographic manifestations of hypopotassemia.

Muscular disturbance, varying from weakness to paralysis, lethargy, delirium, coma, or death. Sagging or depression of S-T segments, flattening or inversion of T-waves, prolongation of QT interval and, arrhythmias.

In what conditions may a deficiency in vitamin A occur?

Chronic diarrhea, obstruction of the biliary ducts, hyperthyroidism, pernicious anemia, pancreatic disease or other disorders of fat metabolism, severe infection, and during periods of rapid growth.

Give the clinical signs of vitamin B_1 deficiency.

Loss of appetite, malnutrition, circulatory failure (edema, serous effusion, cardiac collapse), beriberi, polyneuritis, Korsakow's syndrome, and Wernicke's encephalopathy.

Outline the treatment of pellagra.

(1) Rest in bed during early stages. (2) Removal of cause: most cases result from a faulty diet; others develop as a consequence of some disease (gastrointestinal lesions). (3) Nicotinamide, 100 to 200 mg. orally 3 times daily, or 50 mg. 3 to 5 times daily intramuscularly in severe cases. (4) Brewer's yeast, 1 to 4 tablespoonfuls by mouth 3 times daily, and crude liver extract, 2 to 4 cc. intramuscularly daily. (5) The diet should contain ample protein and, during the early stages, 2,500 to 3,000 calories (which is increased to 5,000 calories as the patient improves and becomes ambulatory). (6) Local treatment to raw surfaces (skin, tongue, etc.). Antimicrobial agents may be of value. (7) In seriously ill patients, ACTH has been used, with reported success, to improve absorption.

Of what value is pyridoxine (vitamin B_6) in INH toxicity?

Pyridoxine deficiency, as manifested by peripheral neuritis, may occur following the use of INH (usually with high doses). Such cases respond well to the oral administration of pyridoxine hydrochloride, 50 mg. 3 times daily.

Outline the prophylaxis of rickets.

For the most part, an adequate vitamin D intake and exposure to sunlight are the preventive measures. The amount of vitamin D required varies with the age of the individual (premature infants need more) and the amount of sunlight. In general, 400 to 800 international units of vitamin D (irradiated milk, cod liver oil, fish oil concentrates, or synthetic preparations) will prove effective.

DISEASES OF THE CARDIOVASCULAR SYSTEM

Give a practical classification of diseases of the heart.

The classification of heart disease as outlined by the American Heart Association is recognized and widely used. The accepted form is:

1. *Etiology:* Rheumatic fever, syphilis, arteriosclerosis, hypertension, hyperthyroidism, congenital.
   Aortic aneurysm, coronary thrombosis, cardiac enlargement, subacute bacterial endocarditis, aortic insufficiency, mitral stenosis, chronic constrictive pericarditis.
2. *Physiological Diagnosis:* Atrial (auricular) fibrillation, complete A-V block, paroxysmal atrial (auricular) tachycardia, premature ventricular contractions, valvular incompetence.
3. *Functional Capacity:* (*a*) Ordinary physical activity causes no discomfort. (*b*) Ordinary physical activity causes discomfort. (*c*) Less than ordinary physical activity causes discomfort. (*d*) Any physical activity causes discomfort.
4. *Therapeutic Classification:* (*a*) No restriction. (*b*) No unusually severe effort. (*c*) Moderate restriction of ordinary activity. (*d*) Marked restriction of ordinary activity. (*e*) At complete rest.
5. *Potential Heart Disease.*
6. *Possible Heart Disease.*

Give the area of normal heart dulness. What conditions increase the area of heart dulness?

The *superficial* cardiac dulness extends from the fourth rib above to the sixth rib, merging with the liver dulness. The right border coincides with the left edge of the sternum; the left border is parallel to, and about 2 cm. inside, the left midclavicular line.

The *deep* cardiac dulness (generally used in percussion of the heart) is bounded above by the lower border of the third rib or the third intercostal space. The left border corresponds to the left midclavicular line; the right border is from 2.5 to 3.5 cm. from the midsternal line.

The dulness is increased in cardiac enlargement due to dilatation or hypertrophy; pericarditis and pericardial effusion; mediastinal tumor; aneurysm of the thoracic aorta; pleural effusion; tumor of heart and pericardium.

What are hemic murmurs as applied to the heart, and what is their cause?

Hemic murmurs occur in anemia and are held to be due to some alteration in the constitution of the blood and to diminished blood pressure. They are practically always systolic, soft, and blowing, heard at or near the pulmonary cartilage, and not transmitted.

State where topographically mitral and tricuspid murmurs are most distinctly heard.

Mitral regurgitant, in mitral area.

Mitral stenotic, at or just inside position of apex beat.

Tricuspid regurgitant, at or a little to the right of ensiform cartilage.

Tricuspid stenotic, same situation as mitral stenotic.

List the etiologic factors in chronic valvular cardiac disease and give examples of each.

(*a*) Congenital—pulmonic stenosis. (*b*) Rheumatic—mitral stenosis. (*c*) Syphilitic—aortic regurgitation. (*d*) Bacterial endocarditis—mitral regurgitation. (*e*) Arteriosclerotic—aortic stenosis.

Give the physical signs of the most usual valvular lesion of the heart.

The physical signs of *mitral regurgitation* are:

Inspection: Displacement of apex beat to the left and, rarely, downward.

Palpation: Thrill is rare; systolic when present. Pulse small and soft; after failure of compensation, irregular and unequal.

Percussion: Cardiac dulness increased transversely.

Auscultation: Systolic murmur heard best at the apex and transmitted to the axilla and the angle of the scapula. Variable in character, sometimes musical. Accentuation of second pulmonic sound.

Why is dyspnea caused by disorganization of the mitral valves?

Because incompetence of the mitral valve leads to dilatation of the left atrium and engorgement of the lungs, followed by dilatation of the right heart, which still further increases the pulmonary congestion.

What are the physical signs of stenosis of the mitral valve?

Inspection: Bulging of the precordia (in children). Engorgement of veins in the neck and thorax. Apex beat not displaced.

Palpation: Presystolic thrill in fourth or fifth interspace inside of nipple lines. Systolic shock. Cardiac impulse left at lower edge of sternum. The characteristic pulse is small and irregular in force and rhythm.

Percussion: Cardiac dulness increased slightly in transverse diameter and upward.

Auscultation: Rough, *presystolic* murmur inside the position of the apex beat; not transmitted. Second pulmonic accentuated or reduplicated.

What are the physical signs of aortic regurgitation?

Inspection: Apex beat displaced downward and to the left; area of impulse increased. Pulsation of carotids, temporals, brachials, radials, and aorta (at suprasternal notch and in epigastrium). Capillary pulse.

Palpation: Confirms inspection; diastolic thrill may be felt over sternum. Corrigan pulse.

Percussion: Reveals great enlargement of cardiac dulness (*cor bovinum*).

Auscultation: Diastolic murmur at aortic area transmitted down the left side of sternum. Absence of second aortic sound. Flint murmur may be present.

Pulsation of retinal arteries. Double murmurs heard over arteries.

Wide pulse pressure.

Differentiate aortic and mitral valvular diseases.

Aortic disease is characterized by hypertrophy of the left ventricle, recognized by downward and outward displacement of apex beat. The pulse is characteristic: *Corrigan pulse* in regurgitation, and slow (*pulsus tardus*) in obstruction. Aortic murmurs are heard best at the second right costal cartilage and are transmitted into the neck (obstruction) or down the sternum (regurgitation). In *mitral regurgitation* the murmur is systolic and transmitted to axilla and angle of scapula; the presystolic murmur of *mitral stenosis* is not transmitted and is accompanied by a thrill. The second pulmonic murmur is accentuated and the pulse is not characteristic, except that it is more frequently irregular than in aortic lesions.

Differentiate organic and functional heart murmurs.

ORGANIC	FUNCTIONAL
Systolic, presystolic, or diastolic, depending on lesion.	Practically always systolic.
Constant; not abolished by posture or respiration, although may be modified in intensity.	Inconstant: heard at one examination and absent at the next. Often disappear on change of posture or on holding breath.
Variable in character: blowing, rough, prolonged, short—depending on lesion.	Almost always soft and blowing, usually short.
Intensified by exercise, never abolished.	Sometimes abolished by exercise ("musculovalvular" murmur).
Cannot be made to disappear.	"Cardiorespiratory" murmurs disappear when breath is held, and often on change of posture while breathing.
Heard best at definite points (points of maximum intensity) according to lesion, and transmitted in definite directions.	Heard most commonly at pulmonary area, or at mitral, very rarely at aortic. Not transmitted.
Thrill sometimes present (in obstructive lesions).	Absent.
Evidence of cardiac enlargement.	No enlargement.
Usually history of previous infection (rheumatism, syphilis).	Usually none.

Discuss the factors involved in selecting patients with mitral stenosis for commissurotomy.

(*1*) *Age:* Most patients who develop difficulty due to "pure" mitral stenosis do so between the ages of 30 and 45 years. Most patients in their teens who develop serious rheumatic cardiac disability prove to have complicating rheumatic activity, severe mitral insufficiency, multiple valvular involvement, myocardial disease, marked cardiac enlargement, or a combination of these. In patients over fifty, the surgical risk is increased.

(*2*) *Rheumatic Activity:* Clinical evidence of active rheumatic fever or carditis is considered an absolute contraindication to mitral commissurotomy.

(*3*) *Persistent Congestive Failure:* Most patients who remain in severe "right-sided" congestive failure despite intensive medical therapy cannot be improved by surgery because of irreversible changes in the pulmonary circulation. However, occasionally such a patient is improved remarkably after surgery.

(*4*) *Apical Systolic Murmurs:* Formerly, apical systolic murmurs were thought to represent mitral insufficiency of a degree sufficient to contraindicate mitral commissurotomy. However, in many instances, despite such murmurs, the patients have proved to have severe mitral stenosis without significant insufficiency and have derived great benefit from mitral commissurotomy.

(5) *Aortic Valvular Disease:* Under most circumstances aortic insufficiency represents a contraindication for mitral commissurotomy. If the diastolic blood pressure is not significantly widened, the presence of a basal diastolic murmur of semilunar valvular insufficiency is not necessarily an absolute contraindication for mitral commissurotomy. Aortic stenosis, on the other hand, does not now represent so serious a problem, since the development of surgical techniques for its relief.

(6) *Pregnancy:* With good medical management, many patients with mitral stenosis do well during pregnancy; hence, unless absolutely necessary, valvulotomy should be postponed. If indicated, the operation should be performed before the seventh month.

(7) *Valvular Calcification:* In general, calcification of the mitral valve is an unfavorable finding and may well have an adverse influence on the success of the surgical procedure. It does not, however, constitute a contraindication to operation.

(8) *Subacute Bacterial Endocarditis:* When active, this disease represents a contraindication to operation. However, mitral commissurotomy might be undertaken in those patients after the bacterial endocarditis is cured.

(9) *Atrial Fibrillation:* The presence of this arrhythmia is not considered a contraindication to operation. These patients do very well provided the ventricular rate can be kept under good control by digitalization.

(10) *Arterial Embolism:* Previous embolisms, if not too crippling, do not represent a contraindication to operation. In fact, repeated embolism actually may constitute an indication for mitral commissurotomy even in the absence of significant cardiac failure.

List the common diagnostic errors associated with mitral stenosis.

(1) *Bronchial Asthma:* In certain patients with mitral stenosis, the stage of pulmonary congestion is accompanied by a prominent element of bronchial spasm with wheezing.

(2) *Pulmonary Disease:* Mitral stenosis may cause a chronic cough, with or without hemoptysis and pulmonary rales.

(3) *Thyrotoxicosis:* Weight loss, nervousness, excessive sweating, and tachycardia may occur in patients with mitral stenosis.

(4) *Neurasthenia:* Certain patients with mitral stenosis complain chiefly of weakness, easy fatigue, and other vague symptoms. They may be thin and nervous and have cold hands.

Describe the characteristics and significance of the several kinds of arterial pulse.

Normal: Regular 70 to 80 a minute in the adult; moderately full and strong.

Intermittent: Loss of one or several beats at regular or irregular intervals. May be normal; occurs in tobacco heart, fatty degeneration, and "weak heart."

Irregular: Both in rhythm and volume. Common in myocarditis and in mitral lesions.

Bigeminal or Trigeminal: Two or three beats followed by a longer pause. Same significance as irregular.

Corrigan: Short, quick, and receding. Characteristic of aortic regurgitation.

Dicrotic: Main beat followed by a secondary beat or wave; indicative of low tension. Seen in asthenic fevers, especially typhoid.

Pulsus Paradoxus: Pulse suppressed at the end of inspiration. Observed in adherent pericardium.

Pulsus Alternans: Alternate strong and weak beats with normal cardiac rhythm. Indicative of advanced degeneration of the myocardium and a grave prognosis.

Discuss the value of electrocardiography in the practice of medicine.

Electrocardiography has been the means of greatly increasing the accuracy of cardiac diagnosis and prognosis and of affording some valuable indications for treatment. In evaluating its usefulness, certain facts must be borne in mind.

An electrocardiogram is a record of the electrical behavior of the heart at the moment the electrocardiogram is taken and, like pulse rate, blood pressure, and other cardiac factors, varies at different times. Hence a normal tracing does not necessarily indicate the absence of disease and, conversely, positive findings may be obtained in normal hearts. Differences in tracings taken at different times, even when slight, are, however, regarded as significant of myocardial impairment. When the heart is normal, the character of the electrocardiogram is likely to be constant.

For the purpose of diagnosis the method is pathognomonic of certain disorders including myocardial infarction and the various arrhythmias. It is extremely valuable in the diagnosis of pulmonary infarction, pericarditis, and myocardial damage. Although electrocardiography may uncover otherwise undetectable abnormalities, serious cardiac diseases may exist in the absence of electrocardiographic changes.

The electrocardiograph is useful for detecting certain chemical changes in the blood and in the study of the effects of drugs, notably digitalis and quinidine.

What has been said about electrocardiography in diagnosis applies equally to prognosis. The existence of certain abnormalities of rhythm detected with the electrocardiograph may influence the *prognosis* in a given case of heart disease. Thus, bundle branch block, especially of the left branch, is generally regarded as an unfavorable finding.

Give the formula of, or show by diagram, ventricular preponderance or axis deviation.

Highest upward deflection (R_1) in Lead I and lowest downward deflection (S_3) in Lead III denotes *left ventricular preponderance* or left axis deviation.

Lowest downward deflection (S_1) in Lead I and highest upward deflection (R_3) in Lead III denotes *right ventricular preponderance* or right axis deviation.

What effects have large doses of digitalis on the electrocardiogram?

(1) Lengthening of the P-R interval (conduction time).

(2) Depression of the RST segment, with inversion of T and formation of the U-shaped depression with concavity directed upward.

(3) Shortening of the Q-T interval.

(4) Production of various arrhythmias, especially premature ventricular contraction and A-V heart block.

The digitalis effect persists for about 2 weeks.

What changes occur in the electrocardiogram with abnormal serum concentrations of potassium or calcium?

In hyperkalemia, the duration of the T wave decreases and the voltage increases, giving rise to a sharp, high T wave. With very high serum potassium levels, the P wave may move close to, or into, the QRS group, and the QRS group may become widened and notched. Hypokalemia tends to produce lengthening of the Q-T segment, with lowering of the T waves. Hypercalcemia produces a shortening of the Q-T interval, with lowering of the T waves, or even negative T waves. Hypocalcemia produces a lengthening of the Q-T intervals but the T waves are not altered.

Mention the significant diagnostic features of the electrocardiogram in a case of acute coronary occlusion with (a) anterior myocardial infarction and (b) posterior myocardial infarction.

(*a*) *Anterior:* Deep Q wave in Lead I and possibly in Lead II; RST segments elevated in Leads I and II, depressed in Lead III, elevated in chest leads.

(*b*) *Posterior:* Deep Q wave in Lead III, often in Lead II; RST segment elevated in Leads II and III, depressed in Lead I, depressed in chest leads. In the subacute and chronic stages the T waves become inverted, the RST segments gradually return to the isoelectric line, and the T waves tend to return to their original upright position.

What special tests are sometimes employed in the diagnosis of heart disease?

(1) Cardiac catheterization, (2) phonocardiography, (3) ballistocardiography, (4) electrokymography, and (5) angiocardiography.

Discuss briefly sinus tachycardia and sinus bradycardia.

Tachycardia: Discharge of impulses from the sinus node is over 100 per minute. It may be a physiological response to exercise, emotional disturbances, eating, drugs, hemorrhage, fever, heart failure, hyperthyroidism, etc. The treatment depends upon the underlying cause.

Bradycardia: Discharge of impulses from the sinus node is less than 60 per minute. It may occur normally, especially in athletes and during sleep. It may be found in malnutrition, jaundice, typhoid fever, intracranial lesions, digitalis effects. The rate increases with exercise. Treatment depends upon the underlying condition. When associated with marked vagal tone the ventricle may "escape."

Define the various forms of cardiac arrhythmia and give a brief description of the disturbance of mechanism and the associated physical signs in the heart and pulse.

Sinus Arrhythmia: Irregularity of the heart due to disturbance in the sinoatrial node interfering with the rhythmic discharge of impulses. It consists in a *gradual acceleration* and *retardation* of the heart rate and affects both the ventricular and pulse rates. Radial beats and apex pulsations correspond. The pulse rate is usually slower than normal. This form is seen mostly in children and young adults and is also called *juvenile arrhythmia* and *respiratory arrythmia,* although it also occurs independently of the respiratory phases. It disappears on exercise.

Although the prognosis is in general favorable, sinus arrhythmia is sometimes observed in old persons with myocardial disease. It may also be due to digitalis.

Premature Contractions: Contractions occurring before the regular time in response to new and isolated (pathological) impulses formed at some point in the atrium or ventricle or in the junctional tissue.

The normal rhythm is interrupted by a *premature contraction* of the heart (in response to a pathological impulse), which occurs before the regular time for the heart beat and is followed by an abnormally long pause. This pause is due to the fact that the heart, after the premature contraction, is in the refractory stage and fails to respond to the next succeeding impulse. The prolonged pause is called the *compensatory pause.* Clinically, premature contractions manifest themselves by "intermittence" of the pulse. At the moment of the premature contraction, a heart beat is heard at the apex before the rhythmic beat is due, followed by an unusually long pause. The premature contraction may be too feeble to raise the aortic valve, in which case only an isolated premature first sound is heard and the pulse beat ("dropped beat") fails completely. The pulse rate is usually slow, under 100. Premature contractions or *extrasystoles* may be atrial, ventricular, or nodal in origin.

In the *atrial type,* the premature P wave in the tracing is usually merged with the preceding T and the ventricular complexes are normal. The following compensatory pause is somewhat less than two cardiac cycles. In the *ventricular type,* the ventricular complexes are greatly distorted, broad, and "slurred" or "notched." R may be upright or inverted depending on the origin of the ectopic impulse in the ventricles. The T wave takes the opposite direction to that of R. Both P and T may be buried in the distorted ventricular complex. When the extrasystoles occur regularly every two or three beats, a bigeminal or trigeminal pulse respectively is produced. The compensatory pause in this form is exactly equal to two cardiac cycles. This condition is sometimes produced by digitalis.

The irregularity is seen most frequently between the ages of 50 and 70 and is much more common in men. It is usually associated with valvular or myocardial disease, often with hypertension; however, it also occurs in apparently normal hearts. Some patients are conscious of the irregularity and describe it as "palpitation," a sense of uneasiness, or a "gone feeling" during the pause, and the sensation of a shock to the chest wall or a choking sensation with the succeeding contraction of the heart. The prognosis is guardedly favorable.

Nodal Rhythm; ATRIOVENTRICULAR OR NODAL ECTOPIC BEATS: The impulse originates in the A-V node or in the bundle of His and passes to atrium and ventricle, reaching one or the other first. In the tracing P is altered in shape and its relation to R varies. There may be an R-P instead of a P-R interval, and this interval varies in length. The ventricular complexes may or may not be altered. It cannot be recognized clinically.

Atrial Fibrillation: A condition in which normal impulse formation in the atrium (sinoatrial node) is replaced by stimulus production at multiple atrial foci.

True contraction of the atrium is replaced by ineffectual twitchings of the chamber; in place of the normal and regular impulses from atrium to ventricle, numerous irregular impulses arising in the atrium reach the ventricle and produce a completely disordered ventricular rhythm. The pulse, as well as the heart beat, is absolutely irregular both in time and volume (*pulsus irregularis perpetuus, delirium cordis*), and the rational signs of cardiac failure are usually (but not always) present. If the pulse can be counted at all, it is usually above 100. Ordinarily it is the easiest of all the arrhythmias to recognize clinically. It is found typically in rheumatic hearts with failing compensation and the classical associated signs—dyspnea, cyanosis, edema, and hepatic engorgement. It is most frequent in persons of advanced years, but occurs, as is well known, in young patients with rheumatic valvular disease. Fibrillation is present in from 60 to 70 per cent of all cases of cardiac failure, due to whatever cause. It is more common in men than in women.

The *prognosis* is always serious and becomes more so if the ventricular rate is persistently high—120 and over—in spite of treatment.

The electrocardiogram is characteristic. Since the atria do not contract, there are no P waves but, instead, very small *fibrillary waves;* the ventricular complexes are normal in shape but occur at very irregular intervals.

In a clinical sense auricular fibrillation is the most important cardiac arrhythmia. It is always a serious condition and it responds very satisfactorily to treatment.

Atrial Flutter: The atrial rate is excessively accelerated—230 to 350—and, as the ventricles cannot respond to all the impulses, partial heart block is associated. The atrioventricular ratio is usually 2:1 or 3:1.

In the electrocardiogram the P waves appear as regularly spaced fine *fibrillations* or as peculiar triangular deflections. The rate is always regular. R waves are normal in shape and are also regularly spaced, but there are usually two or three P waves to one R.

The mechanism of atrial flutter and atrial fibrillation is described as a *circus movement.* The impulse travels around the atria and back to its starting point and sets up a continuous, rapid, and regular rhythm in the atria, the impulse arriving at the starting point when the muscle is able to respond, i.e., is not in the refractory stage. In atrial fibrillation the impulse follows an irregular course and the rhythm is therefore irregular—an *impure* circus movement.

Flutter cannot be diagnosed with certainty without the aid of the electrocardiograph. It is almost always associated with organic disease of the heart.

Heart Block: Three degrees of heart block are recognized:

FIRST-DEGREE HEART BLOCK: This is also called *delayed conduction time.* When the P-R interval exceeds 0.2 second, conduction is said to be delayed. The condition cannot be recognized clinically. It is of some diagnostic importance, as it is found chiefly in rheumatic fever and diphtheria. It is also produced by digitalis.

SECOND-DEGREE OR INCOMPLETE HEART BLOCK: The atrioventricular ratio is quite variable, 2:1, 3:1, or other proportions. Partial block usually produces a slow pulse rate, 40 or under. The diagnosis is difficult without the electrocardiograph, since it may be confused with simple bradycardia or with complete block or even with extrasystoles.

No treatment is necessary for the irregularity itself; but, if digitalis is indicated, it must be given cautiously when incomplete block is present, as it tends to convert a partial into a complete block.

THIRD-DEGREE HEART BLOCK (COMPLETE HEART BLOCK): There is complete dissociation between atrial and ventricular contractions. The atria contract in response to the pacemaker and the ventricles to an impulse originating in the A-V node or the bundle of His at a point below the site of the lesion. The tracing shows the two rates, P and R, which are usually regular or nearly regular, and the complexes are not much altered in shape.

The pulse rate in complete heart block varies from 30 to 50, usually 40 or below.

Heart block can sometimes be recognized clinically without the aid of cardiography: (1) When atrial systole is audible and produces reduplication either of the first sound or of the second sound, depending on the degree of widening of the A-V interval; and, in cases of mitral stenosis, when the characteristic presystolic murmur and the thrill are caused by contraction of the atrium. (2) When the atrial rate can be determined by inspection of the jugular vein, which rarely is seen to pulsate, and the jugular rate is higher (2:1, 3:1) than the ventricular. (3) In cases of "dropped beats" when auscultation at the apex reveals no ventricular contraction during the unusually long pause (intermittence). The influence of respiration must be excluded. (4) Whenever the ventricular rate is 35 or less per minute, as in the condition known as Adams-Stokes syndrome.

Heart block occurs at any age and from the same causes as those of heart disease in general—rheumatism and chorea in younger patients, syphilis, and senile changes. Heart block can be induced by the administration of digitalis.

The lesions most frequently found in the bundle of His are chronic inflammation, fibrosis, calcification, and atrophy.

Bundle Branch Block: The impulse may be blocked in the right or left branch of the bundle of His, a condition that cannot be recognized without the aid of the electrocardiograph. The resulting tracing is quite characteristic, the ventricular complexes resembling those of ventricular extrasystoles or ventricular paroxysmal tachycardia. The QRS is broadened at the base. T is usually prominent and opposite in direction to R. The P waves are inconspicuous or entirely absent. The rhythm in bundle branch block, unless some other arrhythmia is associated, is regular.

The direction of the R spike in Lead I and Lead III is important. When R is upright in Lead I and inverted in Lead III, the block is in the *left* bundle branch; and when this condition is reversed, it indicates a *right* bundle branch block. Left bundle branch block is more common than right, and much more serious. Left block is always indicative of myocardial disease, most frequently coronary disease or hypertensive heart disease. It does not call for any special treatment.

Paroxysmal Tachycardia: In both the atrial and ventricular forms a greatly accelerated but regular rhythm is set up by an ectopic focus in the atria or ventricles respectively.

In *atrial* (*auricular*) tachycardia the heart rate ranges from 150 to 250 or higher per minute and the rhythm is entirely regular, more regular than in normal hearts. The attack comes on suddenly and ends abruptly with a sensation described by the patient as a "thump." In normal or sinus tachycardia the onset and the return to normal rhythm are gradual. In the electrocardiogram the ventricular complexes are unaltered, while the P waves are usually absent—buried in QRST.

The condition can be recognized clinically and occurs both in healthy and diseased hearts.

Ventricular Paroxysmal Tachycardia: The ventricular complexes are distorted, resembling ventricular extrasystoles. The atria may contract normally and independently of the ventricles; or the ectopic impulse may travel back along the junctional tissue to the atria, in which case the P waves are merged in QRST and disappear from the tracing. The rate is usually slower than in atrial tachycardia, from 160 to 180, rarely above 200, and the rhythm is slightly irregular. It is not readily recognized clinically; but the slower rate, slight irregularity, the difference in rate between jugular and ventricular pulsations, and the fact that the paroxysm cannot be arrested by carotid or ocular pressure may sometimes enable one to make the diagnosis without the aid of the electrocardiograph.

Ventricular paroxysmal tachycardia may also occur in healthy hearts but is more frequently associated with cardiac disease, especially coronary artery disease than is the atrial form. Digitalis is not only ineffective but even increases the tachycardia.

Pulsus Alternans: This is a rhythm in which a large beat and a small beat alternate, the intervals between beats being regular. It is a sign of depressed contractility, and is frequently associated with other forms of cardiac irregularity.

Pulsus alternans produces no alterations in the electrocardiogram, for the normal mechanism is not disturbed. It can be diagnosed clinically by noting that every other radial beat is weaker, but must not be confused with premature contraction of every other beat (pulsus bigeminus). In pulsus alternans the intervals between beats are equal, while in bigeminy, due to premature contractions, the pause following the weaker beat is prolonged.

A radial or brachial tracing provides the surest method of showing pulsus alternans. It can also be detected with the aid of the sphygmomanometer by noting that the pulse rate becomes halved at a point just below the systolic pressure.

Pulsus alternans does not occur in normal hearts. It is a sign of myocardial disease and the *prognosis* is always extremely grave.

What are the possible harmful effects of the arrhythmias?

The bradycardias as a rule have little or no clinical significance, unless the rate slows to 15 or less, in which case the circulation to the brain becomes inadequate (Adams-Stokes syndrome); a complete standstill or fibrillation of the ventricles leads to death. The tachycardias cause a diminished cardiac output, interference with the coronary blood flow, and an increase in energy expended by the heart. Hence, tachycardia alone, if sufficiently severe and prolonged, may lead an otherwise healthy heart to fail. Furthermore, irregularity of the heart may prove deleterious when a pulse deficit is present and the ectopic beats occur so early in diastole that the degree of ventricular filling is slight and the energy developed at the contraction is not sufficient to expel a significant amount of blood.

Outline the treatment for paroxysmal atrial tachycardia.

In many instances, the patient may learn to terminate his own attacks by (1) mild sedation with a barbiturate, (2) taking a deep breath and attempting to expire against a closed glottis (Valsalva maneuver), (3) inserting a finger into the pharynx to induce gagging and vomiting, (4) pressure on the eyeballs, (5) massage of the right and then the left carotid-sinus region. The physician may first repeat the Valsalva maneuver and carotid pressure simultaneously. If the attack persists, rapid digitalization is indicated, provided the patient is not already receiving the drug: lanatoside C (Cedilanid), 1 to 1.2 mg. very slowly, intravenously, or oral quinidine, 0.4 gm. every 2 hours for 5 to 6 doses, provided no signs of toxicity to quinidine are present. In desperate instances, acetyl-beta-methylcholine (Mecholyl) is administered subcutaneously or intramuscularly, 5 to 10 mg., and repeated in several minutes (total dosage should not exceed 30 mg.). Atropine sulfate (1 mg.) should be immediately available for possible toxic reactions. Between attacks, treatment consists of: (1) removal of cause, (2) digitalis, or (3) quinidine.

What is the significance of paroxysmal ventricular tachycardia and what is the drug of choice in treatment?

This condition is always associated with myocardial damage, and its continuance predisposes to ventricular fibrillation and sudden death. Procainamide (Pronestyl) is the drug of choice.

What are the indications for the conversion of atrial fibrillation to normal sinus rhythm?

To improve cardiovascular dynamics and to lessen the chance of embolic phenomena. Quinidine is the drug of choice; most patients who will revert to normal rhythm (approximately 50 per cent) usually do so with moderate doses of the drug. The object is to obtain a quinidine plasma level of about 10 mg. per liter. This may be accomplished by the use of 0.5 gm. of quinidine sulfate every 2 hours over a 12-hour period; if normal rhythm is restored, the patient is placed on a maintenance dose of 0.2 gm. every 6 hours for 4 weeks. The possibility of quinidine toxicity should be kept in mind, especially when the concentration reaches a level of 10 mg. per liter.

Give the causes and clinical picture of angina pectoris.

Angina pectoris is not a disease but rather a symptomatic affection resulting from myocardial ischemia associated with an insufficient coronary circulation resulting from coronary artery disease (arteriosclerosis, syphilis), aortic insufficiency or stenosis, severe anemia, paroxysmal tachycardia, or hyperthyroidism. Clinically, the most important feature is that of substernal pain extending into the arms and neck, which is usually brought on by exercise (walking into wind, climbing stairs, etc.) and, less commonly, by eating a large meal, excitement or anger, and sexual intercourse. The patient can frequently define the exact amount of exertion required to produce pain and he is forced to cease the exertion when the pain occurs. With rest, the pain usually disappears within a few minutes. Rarely, the patient may complain only of a sudden feeling of severe weakness on exertion but no pain (anginal equivalent).

Describe the clinical picture and treatment of acute myocardial infarction.

Sudden, severe substernal pain that may radiate down the arms, sweating, pallor, cyanosis, dyspnea, tachycardia, low-grade fever, reduction in blood pressure, ectopic heart beats, pericardial friction sound, systolic murmur, leukocytosis, increased sedimentation rate, elevated serum transaminase concentration, and characteristic electrocardiographic changes, especially when recorded serially. Treatment consists of bed rest, morphine for pain, oxygen in all moderate or severe cases, papaverine or atropine at regular intervals to combat coronary spasm, vasopressor drugs (ephedrine, mephentermine [Wyamine], norepinephrine [Arterenol], etc.) to combat marked hypotension, subcutaneous or slow intravenous feedings if patient cannot tolerate fluids by mouth, and a light bland diet after the first 48 to 72 hours. Anticoagulants are used to reduce the incidence of thromboembolic complications and may prevent propagation of the thrombus or the formation of a new thrombus in the coronary system. There still exists a difference of opinion on whether all patients should receive anticoagulants; some feel that those patients with mild symptoms need not receive these agents. Preexisting hemorrhagic diseases are a definite contraindication to the use of anticoagulants. Likewise, they are generally undesirable in the presence of ulcerated lesions, subacute bacterial endocarditis, hepatic dysfunction, and nephritis. Caution is to be exercised in patients with history of duodenal ulcer or bleeding hemorrhoids. If the prothrombin time is normal, 300 mg. of bishydroxycoumarin (Dicumarol) is given orally as the initial dose, the subsequent daily dosage varying from 0 to 250 mg., depending on the prothrombin time for each day. The object is to maintain the prothrombin level between 20 and 30 per cent of normal. If bleeding occurs, vitamin K (menadione disulfate, 50 mg.) is given intravenously. If the patient is first seen several days after the onset of the disease, heparin (200 mg. in Pitkin menstruum subcutaneously) may be given, since it requires 24 to 48 hours for Dicumarol to attain its maximum effect. Tromexan (ethyl biscoumacetate) produces a more rapid increase (18 to 24 hours) in prothrombin time than does Dicumarol and may be employed instead of the latter. Recently, some workers have advocated repository heparin instead of Dicumarol for routine therapy, in that it has an immediate as well as a prolonged action, and the effect can be easily gauged by the determination of blood-clotting time. Economically, it appears advantageous, as far as the laboratory control is concerned. Regardless of the anticoagulant employed, it is important that the patient be carefully followed with the necessary laboratory studies—clotting time when heparin is used, and prothrombin time with the percentage of normal in those receiving Dicumarol or Tromexan. Anticoagulant therapy is continued for at least 28 days. Digitalis is used in the presence of atrial fibrillation or congestive heart failure. Procainamide (Pronestyl) should be employed for ventricular tachycardia. The duration of complete rest is 4 to 6 weeks or longer in severe attacks attended by failure.

What are the causes and treatment of palpitation of the heart?

Causes: (*a*) Toxic substances: tobacco, coffee, and tea; (*b*) overexertion; (*c*) nervous causes: hysteria, neurasthenia, emotional disturbances; (*d*) failing compensation in valvular and myocardial disease; (*e*) anemia; (*f*) reflex causes: indigestion, dilatation of stomach, flatulence.

Treatment: This depends altogether on the underlying cause, which must, if possible, be removed. Rest and an icebag applied to the precordium are useful measures in most cases.

Give the symptoms and signs of congestive heart failure. What are the general means of treatment?

Findings: Those of passive congestion of various organs: (1) of the lungs—dyspnea, orthopnea, cough, expectoration, cyanosis, basal rales, pleural effusion, reduced vital capacity; (2) of the liver—abdominal discomfort, fulness or pain, indigestion, belching, flatus, anorexia, tender and enlarged liver, occasionally slight jaundice; (3) of the kidneys—oliguria, increased urinary specific gravity, albumin, casts, increased blood urea and nonprotein nitrogen; (4) of the venous circulation—edema, anasarca, prominent neck veins, increased venous pressure, increased circulation time.

Treatment: The burden upon the heart must be reduced, cardiac efficiency improved, and edema eliminated. Rest is of primary importance. Oxygen may be necessary if dyspnea is marked. Diet must be simple, nutritious, easily digestible, and nongaseous. Sodium chloride intake must be reduced to a minimum. Fluids may be given as desired by the patient. Intake and output of fluids should be recorded and the weight followed. Bowel function should be attended to, employing gentle laxatives when necessary. Sedatives are often required to allay anxiety, permit rest, and induce sleep. The value of morphine cannot be overestimated in the treatment of cardiac failure and often is lifesaving. This drug is particularly useful when pain is an associated factor.

Digitalis is preferably used by mouth, 1 cat unit per 10 pounds of body weight, the rapidity of administration depending upon the urgency of the individual case. The maintenance dose is 1 cat unit daily. The most satisfactory oral preparations are the powdered leaf and the glycoside digitoxin. Full digitalization is achieved with approximately 1.5 gm. of digitalis leaf or 1.2 mg. of digitoxin and maintenance with 0.1 gm. of the former and 0.1 or 0.2 mg. of the latter. In the presence of atrial fibrillation the ventricular rate should guide the dosage.

Diuretics are effective aids in water and electrolyte excretion. Both acidifying and mercurial diuretics are employed singly or in combination. Ammonium chloride is given, 2 gm. 3 to 4 times daily plus mercaptomerin (Thiomerin) or merethoxylline procaine (Diurin Procaine), 0.5 to 2.0 ml. subcutaneously or intramuscularly daily until the patient maintains his "dry weight." Administration is then gradually reduced to 2 or 3 times weekly and then doses are given as necessary. Caution must be employed when ridding the body of fluids, as the sodium loss occasionally results in a potassium deficit; at times hyponatremia, "low salt syndrome," follows the use of mercurial diuretics in the face of a low salt intake. Recent experience with the thiazide derivatives, chlorothiazide (Diuril, etc.) suggest that these agents are the most satisfactory oral diuretics now available. Thoracentesis or abdominal paracentesis may be necessary if the effusion is large. Likewise, venesection (125 to 200 cc.) may give relief in instances of severe passive congestion with raised venous pressure.

Define and give a classification of hypertension.

Hypertension may be defined as the more or less persistent elevation of the blood pressure above the accepted range for age, sex, and body weight. There are two kinds of hypertension—the primary or idiopathic type, which is referred to as essential hypertension and which accounts for the great majority of cases; and the secondary type, which occurs as a manifestation of one or another of a variety of pathological states, such as (1) renal hypertension—glomerulonephritis, pyelonephritis, polycystic disease, polyarteritis nodosa, unilateral renal disease, and possibly the toxemias of pregnancy; (2) cardiovascular hypertension—heart failure, aortic regurgitation, arteriosclerosis, coarctation of the aorta, arteriovenous fistula, etc.; (3) endocrine hypertension—adrenal cortical and pituitary dysfunction, pheochromocytoma, etc.; (4) cerebral hypertension—increased intracranial pressure, lesions in brain stem, etc.; (5) physiological hypertension—emotions, pain, exertion.

Differentiate benign from malignant hypertension.

Essential hypertension begins without symptoms and is usually discovered in the course of a routine, so-called "health," or a life insurance examination and may persist for years without symptoms. The patients mostly have passed the half-century mark. The blood pressure, both systolic and diastolic, is high—systolic, 180 to 200 or over; diastolic, 100 and over, except in the senile type associated with arteriosclerosis. Eventually, the symptoms of hypertension develop: headache, dizziness, fatigability, moderate anemia, nocturia, and hyposthenuria (fixed low specific gravity). Occasional traces of albumin and a few hyaline and granular casts are usually found. Changes in the eyegrounds—tortuous arteries with increased light reflex, veins compressed at the crossings—are noted. Death occurs late from heart failure, coronary disease, uremia, or cerebral hemorrhage.

The *malignant* form of hypertension is a necrotizing endarteritis with chronic nephritis and the signs and symptoms of kidney damage—low gravity urine, with albumin and granular casts; nitrogen retention; cardiac hypertrophy; anemia. The changes in the eyegrounds are marked—hemorrhages, exudates, and papilledema. The patients are younger than those with the benign form. The prognosis is poor, death occurring in from one to five years from uremia or cardiovascular disease.

Discuss the treatment of essential hypertension.

Although most patients with hypertension suffer from essential hypertension, the diagnosis should not be made until all causes of secondary hypertension have been excluded.

Treatment: (1) REASSURANCE AND GENERAL MEASURES: Except in extreme cases, an initial high blood pressure reading is not too significant. If the blood pressure is slightly elevated, the patient should be followed at intervals, but no more than is absolutely necessary, and symptomatic treatment should be kept at a minimum. The patient should be acquainted with the fact that an elevated blood pressure does not necessarily mean a shortened life or drastic change in activities. However, the physician must advise against undue stresses and strains. Mild sedation (barbiturates) is employed when rest or sleep is deficient. If the patient is overweight, a suitable diet is prescribed. If it becomes apparent that the disease is progressive, more specific forms of therapy are indicated.

(2) LOW SALT DIETS: The mechanism by means of which low salt diets produce depression of the blood pressure in hypertensive patients is not fully understood, but it seems likely that its effective feature is the low sodium content and that the sodium is somehow involved in the maintenance of the blood pressure at abnormal levels in hypertensive patients. It has been demonstrated that, under the same conditions, the excretion of sodium is greater in normal persons than in hypertensives. There is no real salt-free diet; the most frequently employed diets supply about 0.25 gm. of salt per day. The rice-fruit diet is worthy of trial, although the majority of patients are reluctant to continue it long enough to obtain a possible beneficial effect.

(3) ANTIHYPERTENSIVE DRUGS: Although many drugs have been used in the treatment of hypertension, only a few deserve serious consideration, such as chlorothiazide (Diuril), thiocyanate, veratrum alkaloids, hydrazinophthalazine (Apresoline), hexamethonium compounds, pentolinium (Ansolysen), and *Rauwolfia* alkaloids, e.g., reserpine (Serpasil). Whether a given drug, or a combination of drugs, is effective in a case of hypertension depends largely on therapeutic trial. In many cases of mild to moderate hypertension, chlorothiazide will prove effective. If the blood pressure is not in a satisfactory range within a month, one should proceed to one, or a combination of the other drugs. Such combinations as reserpine plus pentolinium, hexamethonium plus hydrazinophthalazine, and pentolinium plus veratrum have proved the most effective. Of the ganglion-blocking agents, pentolinium appears to be the most effective single drug. Thiocyanate and

veratrum alone are both of limited usefulness. Once treatment is instituted, careful vigilance is required in order to adjust dosage and to detect possible untoward reactions resulting from the use of these agents.

(4) SURGICAL TREATMENT: In certain cases, such as malignant hypertension, rapidly progressive hypertension, especially in young men, and severe persistent headache, surgical procedures such as sympathectomy or bilateral adrenalectomy are indicated.

Discuss the significance of myocarditis.

Inflammation of the myocardium is a definite clinical and pathological entity but remains a mysterious disease, in that its relationship to infections and other systemic diseases is not fully understood. With the exception of its occurrence in diphtheria, acute rheumatic fever, and rickettsial diseases, this disorder is often unrecognized, although it may occur during or following acute upper respiratory-tract infection, acute poliomyelitis, infectious mononucleosis, trichinosis, early syphilis, tuberculosis, sarcoidosis, amyloidosis, scleroderma, beriberi, Guillain-Barré's syndrome, atypical pneumonia of unknown etiology, thyroid dysfunction, etc. In all probability, death which is attributed to peripheral circulatory failure in many of the infectious diseases may be due to myocarditis resulting in a diminution of cardiac output. Furthermore, in those patients who survive infection, the changes in the myocardium may be reversible and heal without residual changes, whereas in others the process may result in myocardial fibrosis, which could ultimately lead to congestive heart failure.

Differentiate a pericardial friction sound from pleurisy without effusion.

Pericardial friction sounds have a characteristic to-and-fro quality and are not influenced by respiration; pleuritic friction sounds disappear when respiration is suspended.

Give the most frequent causes of pericarditis.

Acute: Rheumatic fever, suppurative infections, tuberculosis, uremia, myocardial infarction, virus infection, trauma, neoplasm.

Chronic: Tuberculosis, pneumococcal infection.

What are the symptoms and signs of (*a*) acute fibrinous pericarditis, (*b*) pericarditis with effusion, (*c*) chronic constrictive pericarditis?

(*a*) *Acute Fibrinous Pericarditis:* Chest pain usually not prominent; to-and-fro friction sound usually in fourth and fifth interspaces near sternum, fleeting in character, not transmitted, modified by respiration; fever; tachycardia; dyspnea; electrocardiographic changes—elevated RS-T segments and progressive diminution of T waves.

(*b*) *Pericarditis with Effusion:* Increased venous pressure with distention of neck veins; decreased cardiac output, which lowers systolic pressure; narrow pulse pressure; tachycardia; increased arm-to-tongue circulation time; decreased motion of heart fluoroscopically; paradoxical pulse; decreased heart sounds; dyspnea; orthopnea; cyanosis; fever; localized pain; symptoms and signs of pressure upon surrounding structures—dysphagia, cough; bulging precordium in children; decreased apex impulse, decreased expansion of left chest, friction sound occasionally at base of heart, widening dullness in first and second interspaces, feeble heart sounds; *Ewart's sign* (compression of left lower lobe); pear-shaped silhouette by x-ray.

(*c*) *Chronic Constrictive Pericarditis:* Manifestations are those of inadequate diastolic filling; increased venous pressure, distended neck veins; ascites; peripheral edema; dyspnea; cyanosis; increased prominence of neck veins with inspiration; hepatic enlargement; small pulse, narrow pulse pressure, paradoxical pulse, and heart usually small and rhythm regular. Electrocardiogram shows low voltage of QRS complexes in all leads and low amplitude of T waves; decreased cardiac pulsations fluoroscopically; calcific deposits in pericardium may be present in x-ray.

Make a diagnosis of aneurysm of the descending aorta.

The symptoms and signs peculiar to aneurysm of the descending aorta are: pain between the shoulders; a dull, expansile, pulsating tumor in the left interscapular region, sometimes with erosion of the third to the sixth vertebra. Pressure symptoms: dysphagia, bronchiectasis from pressures on the left bronchus, and sometimes paraplegia from pressure on the spinal cord.

Discuss the etiology, clinical picture, and treatment of cor pulmonale.

The term "cor pulmonale" denotes hypertrophy and eventual failure of the right ventricle consequent to pulmonary hypertension associated with diseases of the lungs. *Symptoms* are largely those of the underlying disease (dyspnea and cyanosis which is often extreme). When right heart failure ensues, the usual findings are distended neck veins, elevated venous pressure, enlarged liver, and edema. *Treatment* is largely directed at the underlying pulmonary disease, since right heart failure often appears to be precipitated by bronchial infection, and suitable antimicrobial therapy should be employed. Digitalis, diuretics, low salt diet, and oxygen are of aid in alleviating the symptoms of right heart failure.

What factors play a role in peripheral vascular disease?

This group of diseases includes conditions in which structural or functional abnormalities of the peripheral blood vessels prevent normal blood flow through the extremities. However, other disorders may exert striking effects on peripheral blood flow, such as certain systemic diseases (anemias, polycythemia vera, thyroid dysfunction, and heart failure), spondylitis, cervical rib (scalenus anticus syndrome), etc.

Differentiate between intermittent claudication and rest pain.

Intermittent claudication: This is characterized by aching or constricting pain of any group of muscles, especially the calf muscles. It appears after exercise and is promptly relieved by rest. In the absence of anemia, intermittent claudication is indicative of structural arterial disease.

Rest pain: In contrast to intermittent claudication, rest pain is not relieved by rest and is usually worse at night. It accompanies ischemic neuritis, indolent ulcerative gangrene, sudden arterial occlusion by embolism, thrombosis, etc.

Differentiate between gangrene due to arteriosclerosis, thromboangiitis obliterans (Buerger's disease), and Raynaud's disease.

Arteriosclerosis: Advanced age; the history may suggest diabetes; claudication; gangrene may be unilateral; evidence of sclerosis of other arteries; diminished or absent arterial pulsation in the extremities; evidence of damaged heart and kidneys.

Thromboangiitis Obliterans (Buerger's Disease): Occurs in individuals, usually males, of 20 to 40 years of age, often of Jewish race. History of local pain and swelling; claudication; development of small ulcers. Arterial pulsations are absent in the affected extremities; phlebitis is often present.

Raynaud's Disease: Seen most frequently in women. Symmetrical distribution; attacks of pallor, cyanosis, or redness with pain increased by cold or by nervous excitement and relieved by warmth; gangrene is confined to the skin. The nose and ears are sometimes involved. The symptoms are relieved by sympathectomy.

Outline the treatment for motion sickness (air- or seasickness).

(1) Place head firmly against back of seat, preferably in a head rest. (2) Keep eyes on a definite object in space, thus preventing the gaze from shifting with

the position of the boat or airplane. (3) Such drugs as Dramamine and Bonamine are employed successfully.

What is the significance of thrombophlebitis in relation to malignant lesions?

Many instances of thrombophlebitis occur as complications of obvious or far-advanced cancer. However, it may occur before any specific signs and symptoms of malignant disease are apparent, particularly in cases of carcinoma involving the body or tail of the pancreas, and this may serve as an important diagnostic finding. The pathogenesis of this type of thrombophlebitis is not fully understood. In view of the multiple and distant sites involved, miliary metastatic implantation of neoplastic cells on the venous walls, serving as a nidus of formation of a thrombosis, has been considered as a possibility. However, since most of the individual episodes of thrombophlebitis clear up completely, metastatic involvement of the wall seems unlikely. Some have suggested that destruction of tissue leads to the release of an excess of thromboplastin. Others have reported that the adhesiveness of the blood platelets in certain cases of cancer was persistently high, which may result from the action of thrombocytosin, a lipid of body fat that is probably liberated by proteolytic or lipolytic enzymes activated by the breakdown of tissue, such as occurs in malignant disease of any type. Hence, in cases of pancreatic carcinoma, the increased circulatory lipase may contribute even more to the mobilization of thrombocytosin. When instances of thrombophlebitis are encountered, an attempt should be made to exclude primary types, such as that of thromboangiitis obliterans, recurrent idiopathic thrombophlebitis (thrombophlebitis migrans), and all other possible secondary varieties of thrombophlebitis. Thromboangiitis obliterans is characterized by arterial insufficiency with or without thrombophlebitis, by a more chronic course, and by onset usually before the age of 40. Recurrent idiopathic thrombophlebitis usually runs a protracted course that may be episodic over many years, the average age being 40. In thrombophlebitis associated with malignant lesions, the course is usually rapid and the age of the patient is usually over 40. Secondary causes of thrombophlebitis include local factors (clinical or mechanical injury, suppurative or nonsuppurative inflammation, varicose veins, and ischemia) and systemic processes (infectious diseases, blood dyscrasias, pregnancy, postpartum and postoperative states, etc.).

Outline the management of a case of electric shock.

(1) Free patient from the current. (2) Artificial respiration: "back pressure-arm lift" or "prone pressure" method. (3) Spinal puncture, if indicated, for persistent headache or signs of increased cerebral pressure. (4) Epinephrine and other stimulating drugs are of no value and may prove disastrous, in that they may induce ventricular fibrillation and death.

Differentiate between heat exhaustion, heat stroke, and heat cramp.

Heat exhaustion is a physiological breakdown after exposure to heat and is characterized by a peripheral vasomotor collapse. Heat stroke has for its distinguishing manifestation an extreme elevation of body temperature. Heat cramps result from excessive salt loss from the body, giving rise to muscular cramps.

Discuss long-term anticoagulant therapy.

Long-term anticoagulant therapy can now be safely employed for unlimited periods of time, provided that a reliable control technique is used and the treatment is conducted carefully and conscientiously by the laboratory, the physician, and the patient. Most physicians agree that this form of therapy is indicated: (1) in patients with myocardial infarction who have had no more than one attack with no angina, or with angina for less than 2 years; and (2) in patients with angina pectoris of less than 2 years' duration. The value of long-term anticoagulant treatment is far from agreed upon in patients with: (1) chronic rheumatic heart disease; (2) atherosclerosis in the legs without symptoms or signs of coronary or cerebral atherosclerosis; and (3) intermittent insufficiency of the cerebral circulation, presumably due to thrombosis.

DISEASES OF THE UROGENITAL SYSTEM

Give a classification of kidney diseases.

(1) *Nephrosis:* Damage chiefly to the tubules.
  (*a*) Simple; accompanies febrile diseases.
  (*b*) Necrotic; metallic poisoning (mercury).
  (*c*) Eclamptic; nephrosis of pregnancy.
  (*d*) Lipoid nephrosis.
  (*e*) Amyloid nephrosis; associated with chronic wasting diseases.
  (*f*) Cholemic nephrosis; associated with diseases of the liver.
(2) *Glomerulonephritis:* Damage to the glomeruli and small blood vessels.
  (*a*) Focal embolic; as in subacute bacterial endocarditis.
  (*b*) Focal nonembolic.
  (*c*) Acute diffuse.
  (*d*) Subacute.
  (*e*) Chronic.
(3) *Nephrosclerosis* (*arteriosclerotic kidney*): blood vessels affected.
  (*a*) Focal; sclerosis of large vessels.
  (*b*) Simple arteriolar; benign hypertension.
  (*c*) Malignant arteriolar; malignant hypertension.
(4) *Infections.*
  (*a*) Pyelitis, tuberculous and pyogenic.
  (*b*) Abscess.
(5) *Congenital defects:* Polycystic kidney, horseshoe kidney, aberrant vessels, ptosis (movable kidney).
(6) *Tumors:* Hypernephroma and metastatic growths, sarcoma.
(7) *Stone* (*nephrolithiasis*): Infection, obstruction, hyperparathyroid disease, vitamin deficiency.
(8) *Hydronephrosis, pyonephrosis,* and *abscess of the kidney.*
(9) *Injuries of the kidney.*
(10) *Circulatory disturbance.*
  (*a*) Chronic passive congestion.
  (*b*) Infarcts.

Define hydronephrosis. State its causes and describe its treatment.

Distention of the pelvis of the kidney with an accumulation of watery fluid resulting from obstruction in some part of the genitourinary tract, the ureter, bladder, or urethra.

Causes: (1) Congenital stricture of the ureter, (2) inflammatory stricture of the ureter or urethra, (3) impacted calculus, (4) tumors pressing on the ureter or urethra, and (5) movable kidney.

Treatment: Removal of cause. Position and massage may induce evacuation of the fluid; aspiration if the sac is large; draining the pelvis of the kidney after cystoscopy and introduction of ureteral catheter.

Surgical: Establishment of a fistula or extirpation.

Describe pyuria and state its importance.

Pus in the urine. It indicates suppuration in some part of the genitourinary tract or rupture of an abscess into the tract. *Pus derived from the kidney* is intimately mixed with the urine, and the latter has an acid or neutral reaction; *pus from the bladder* is less intimately mixed with the urine, which is usually alkaline. Pyuria occurs in urethritis, cystitis, pyelitis, and pyelonephritis; in salpingitis, extrauterine pregnancy, psoas abscess, etc.

What is the practical import of hematuria and how can its source be diagnosed?

Hematuria is a symptom of disease of the kidneys, bladder, or urethra. It is constant in renal calculus. *Blood from the kidney* is intimately mixed with the urine, which is reddish brown and usually contains casts and renal epithelium. The red blood cells are found singly, and are pale yellow from having lost their hemoglobin. *Hemorrhage from the bladder* is usually more copious, the blood is not intimately mixed with the urine, which, upon standing, shows fibrin. Micturition is frequent and accompanied by pain. In calculus or tumor of the bladder the hematuria is intermittent. In lesions of the urethra or neck of the bladder only the last few drops are bloody. In doubtful cases the cystoscope should be used.

Give the signs and symptoms of floating kidney.

Aside from neurasthenia, which is often present, the *symptoms* are due to the dragging of the kidney on blood vessels and nerves and to pressure upon adjacent organs. The pain comes on in attacks, known as *Dietl's crises,* and is sometimes accompanied by nausea and vomiting. During a crisis the urine is scanty and hydronephrosis may develop; as the kidney returns to its place the twisting of the ureter is relieved and a copious discharge of urine takes place. The kidney can be felt by *bimanual palpation,* coming down during deep inspiration and slipping back into place as the diaphragm returns to the expiratory position. The patient may be aware of the presence of a "tumor" in the abdomen. Usually the signs of enteroptosis are present also; there is diastasis of the recti muscles (Weber's sign), and the eleventh rib is movable (Stiller's sign). Jaundice is sometimes present.

Make a differential diagnosis between renal colic and hepatic colic.

RENAL COLIC

Pain begins in the back and radiates down the ureter into the penis, testicle, and thigh.
Retraction of testicle on affected side.
Hematuria.
No jaundice.
No relation to the taking of food.
Vomiting may or may not occur at the onset.
Stone may be found in the urine.

HEPATIC COLIC

Pain over the liver radiating to the back and to the right shoulder.
Not present.
Urine contains bile, but no blood.
Jaundice may be present.
Usually occurs an hour or two after eating.
Vomiting persistent.
Stone may be found in the stools.

Describe and give the significance of the various pathways of development of urinary-tract infections.

In general, there are three possible pathways or mechanisms of development of urinary-tract infections: hematogenous, contiguous, and retrograde. Obviously, these various routes or pathways by which the organisms invade the urinary tract are very important, in that they serve to indicate the location of infectious reservoirs which must be considered in the light of ultimate treatment.

Any localized infection is potentially a focus, from which bacteria, their toxins, or other dissoluted products may at any time spread via the contiguous tissues, bloodstream, and lymph channels to induce an infection in communicating or distant tissues or to sensitize them. It is unreasonable to expect, therefore, that the removal of focal infections will eliminate a well-established disease process that is characterized by fibrosis or tissue necrosis. Nevertheless, it is important to search carefully in hope of detecting a possible focus of infection. No doubt many potential or established foci of infection may and can be successfully eradicated with the use of the antimicrobial agents alone. For this reason, many unrecognized foci of infection are eradicated without their exact location or nature being known. In a recent survey of the incidence of pyelonephritis during the antibiotic era, a significant decrease in the frequency of its occurrences in autopsies within recent years was revealed.

Since approximately 95 per cent of urinary-tract infections are associated with bacteriological incitants that are normally indigenous to the alimentary canal, a great deal of attention has been given to this area as a possible route of urinary contamination. Evidence has been presented showing a definite correlation between the urinary and fecal flora, which suggests that the feces probably represents a major source of resistant strains isolated in the urine after therapy. Furthermore, studies dealing with diabetic females in particular stressed the importance of perineal hygienic measures as a precaution against reinfection of the urinary tract. Likewise, actual pathological changes in the urinary tract may result from complications of the colon, such as diverticulitis, extraperitoneal appendicitis, and regional enteritis. In such instances, active therapeutic treatment is directed toward the bowel, for the urinary complication will usually disappear after bowel surgery and regression is thereby anticipated in all but the very chronic cases, since the major bacteriological process is not intrinsic in the urinary tract.

What is the significance of pyelonephritis?

With the exception of infections involving the respiratory tract, urinary-tract infections are the most common diseases in the practice of medicine, but information concerning the incidence, pathogenesis, and natural history of pyelonephritis and related infections of the urinary tract is surprisingly incomplete. However, certain aspects of the disease are reasonably well established: Pyelonephritis is found in about 20 per cent of autopsies and represents the most common renal lesion found at autopsy; it occurs about 4 times as often in diabetics as in nondiabetics; it is one of the most common complications of pregnancy; it occurs in about one fifth of the cases of toxemia of pregnancy; it is one of the most common renal lesions in uremia; it is a more frequent cause of Bright's disease than chronic glomerulonephritis; it appears to be etiologically related to malignant and possibly benign hypertension.

What is the significance of persistent or recurrent infections of the urinary tract?

Urinary Stasis: It is well recognized that complete recovery from urinary-tract infection is not to be expected until appropriate measures have been taken to remove all pathological lesions or remedy any condition that interferes with free urinary drainage.

Employment of Improper Antimicrobial Agent: The organism should be properly identified and sensitivity studies performed before switching blindly from one drug to another.

Inadequate Dosage of Antimicrobial Agent: In urinary-tract infections, the offending organisms are present not only in the involved tissue but also in the urine. Obviously, removal of organisms from one site and not from the other will, at best, result only in temporary remission of the infection. Quite frequently, the selection of an antibacterial agent for use in a urinary-tract infection is based on the demonstration that it is excreted in the urine in high concentration and consequently can be expected to be effective. This assumption is probably valid if the primary intention is to sterilize the urine. It should be remembered, however, that recommendations as to dosage are based on *in vitro* laboratory determinations of the urinary concentration of antibacterial agents which inhibits various test organisms. Since substances excreted by the kidney are more concentrated in the urine than in the blood serum or tissue fluids, the demonstration of an inhibitory urinary concentration is no guarantee of the existence of a therapeutic blood or tissue concentration. Hence, the selection of an antibacterial agent and the dosage in which it is to be used should be based not only on the attainable urinary concentration but also on the attainable tissue concentration. The existence of barriers, such as round-cell infiltrations, cicatrices, impaired renal function, or vascularization, militates against effective saturation of the tissue with the antibacterial agent and must also be considered. Certainly, the criteria of cure rest on a long-term follow-up, for in no other group of infections do we see subjective improvement in the face of continued objective findings, such as often occurs in urinary-tract infections.

Development of Drug-Resistant Organisms, or Superinfections: These are likewise resistant to the therapy employed.

Give the antimicrobial therapy of acute pyelonephritis.

The great majority of cases are caused by the micrococcus (staphylococcus), especially in children, and *Escherichia coli* infections, which are often blood-borne and are treated as systemic diseases. When the micrococcus is the causative agent, or when the etiological agent is unknown, the patient should receive aqueous penicillin intramuscularly (300,000 units every 4 to 6 hours), combined with erythromycin by mouth (400 mg. every 4 to 6 hours). In general, the sulfonamides, particularly the sulfapyrimidines (sulfadiazine, sulfamerazine, sulfamethazine), either singly or in combination, or one of the more soluble compounds (sulfisoxazole [Gantrisin], sulfamethylthiadiazole [Thiosulfil], sulfadimetine [Elkosin]), have proved highly satisfactory when the infection is due to *E. coli*. Changes in bacterial flora following widespread antimicrobial therapy have given rise to an increased incidence of acute pyelonephritis due to *Proteus* and *Pseudomonas* infection, which often represent real therapeutic problems. *Proteus* infection is best treated orally with chloramphenicol (250 mg. every 6 hours), or sulfisoxazole (1 gm. every 6 hours), or nitrofurantoin (Furadantin) (100 mg. every 6 hours). Infections due to *Pseudomonas* offer the greatest challenge, as the bacillus is often resistant to all of the antimicrobial agents. A combination of tetracycline by mouth (250 mg. every 6 hours) and streptomycin intramuscularly (0.5 gm. daily) probably is the best form of therapy. If necessary, polymyxin B intramuscularly (20 mg. every 6 hours) instead of the streptomycin for a limited period may prove more effective. On occasion, especially after prostatic or rectal surgery, the infection is caused by the enterococcus (*Streptococcus faecalis*) and responds best to methenamine mandelate (Mandelamine) (3 gm. 3 to 4 times daily) or tetracycline or nitrofurantoin by mouth.

Define pneumaturia.

Pneumaturia is the passage of urine containing air or gas. It may occur after injection of air into the bladder for diagnostic purposes, as a result of a vesicovaginal or vesico-intestinal fistula, or from the presence of gas-forming bacteria in the bladder or urinary tract.

What is the significance of pyuria with sterile urine cultures?

Tuberculosis must be ruled out.

What is meant by renal glycosuria?

A condition of the kidneys in which glucose appears in the urine, even when there is no hyperglycemia, i.e., the threshold of renal permeability is low and glycosuria is present because the kidneys are unable to hold back the blood glucose. This may occur in normal persons or in cases of renal disease, but does not constitute true diabetes. The glycosuria is not influenced by the quantity of carbohydrates ingested, and symptoms of diabetes are absent.

Discuss the etiology of impotence.

Although impotence is a symptom of androgen deficiency and of genitourinary or neurological disease, it is in many instances psychic in origin, especially when it is the principal complaint. Also, notable causes of impotence are the ganglion-blocking agents, such as used in the therapy of hypertension.

Describe the clinical features of acute glomerulonephritis.

In mild cases there is but little constitutional disturbance; the more severe cases may begin with chill, pain in the limbs, fever, and headache. There is hypertrophy of the left ventricle, with increased blood pressure and accentuation of the second aortic sound; later, edema, with effusion into the various serous cavities, and anemia develop.

Urine: The quantity is diminished; the color is dark, the specific gravity high; a small amount of albumin is present, with epithelial and blood casts and sometimes blood. Severe cases show a large amount of albumin and an abundance of hyaline, granular, epithelial, and blood casts, with free blood cells and renal epithelium. The urinary chlorides are diminished and blood chemistry shows retention of nitrogen. At autopsy the kidneys are found to be atrophic and granular.

Enumerate the points of value in the diagnosis of a case of chronic glomerulonephritis.

(1) Insidious onset of edema, which is primarily dependent in nature; (2) recurrent headache; (3) shortness of breath, which may be exertional or paroxysmal in nature; (4) polyuria; (5) hypertension; (6) accentuation of the second aortic sound; (7) hypertrophy of left ventricle; (8) albuminuria; (9) microscopic hematuria; (10) cylindruria; (11) low specific gravity of urine.

Define and give a classification of uremia.

Uremia is a symptom complex that occurs with two characteristic features of renal failure—water and electrolyte imbalance and retention of metabolites. The symptoms are extremely variable: headache, vertigo, delirium, convulsions, coma, sudden blindness, and temporary paralysis from edema of the brain or cord. Dyspnea and Cheyne-Stokes breathing, obstinate vomiting, and purging may be present. The important diagnostic points are dryness of the skin, urinous odor of the breath, and low specific gravity of the urine, which usually contains some albumin and is deficient in urea. The temperature is usually subnormal but may rise during convulsions.

In general, uremia may be classified as (1) prerenal uremia, present in conditions that affect the renal blood supply (hemorrhage, shock, lesions of the vascular supply of the kidney, etc.); (2) renal uremia, resulting from damage to the functioning kidney elements (chronic glomerulonephritis, polycystic disease, bilateral cortical necrosis, acute poisoning, etc.); (3) postrenal uremia, found in advanced obstructive uropathies (prostatic hypertrophy, stricture of the urethra, calculus disease) and as a result of tubular damage ("lower nephron nephrosis") due to severe shock (crush injuries, transfusion reactions, etc.).

Give the indications for dialysis (artificial kidney) in the treatment of uremia.

(1) Severe potassium intoxication, which threatens life and has not responded to simple measures; (2) severe symptomatic acidosis; (3) hyponatremia with a tendency to the formation of pulmonary edema; and (4) a severe uremic syndrome with mental disturbances.

Give the causes, clinical picture and treatment of the nephrotic syndrome.

This syndrome can be caused by a series of widely different underlying disease processes. True nephrosis, which is usually seen in children, is thought to be the result of a disturbance in lipoid metabolism ("lipoid nephrosis"), although the exact mechanism is uncertain. In adults the most common cause of the nephrotic syndrome is chronic glomerulonephritis, but it may occur in intercapillary glomerulosclerosis (Kimmelstiel-Wilson's disease), amyloidosis, secondary syphilis, lupus erythematosus, renal vein thrombosis, and trimethadione (Tridione) toxicity. Clinically, the syndrome is characterized by edema, massive albuminuria, hypoproteinemia, hypercholesterolemia, and, commonly, a lowered basal metabolic rate. The symptoms are related to edema—dyspnea and orthopnea resulting from bilateral hydrothorax and ascites. Malnutrition follows a loss in appetite and is an important factor in causing death. The duration of the nephrotic syndrome is variable and unpredictable. In some instances the syndrome resolves and is replaced by chronic latent glomerulonephritis; in others, signs of rapidly progressive glomerular occlusion occur, ending in renal failure. Susceptibility to infections, particularly pneumococcic peritonitis, is common. Treatment is directed, for the most part, toward the removal of the edema and, when possible, of the underlying disease—syphilis, diabetes, Tridione toxicity, etc. Methods for the elimination of the edema include a high caloric and high protein diet; restriction of sodium; limited fluid intake; plasma expanders, such as infusion of dextrose or salt-free human albumin; and thoracentesis and abdominal paracentesis when necessary. With massive edema, one may be forced to use a mercurial diuretic, although many workers consider this method definitely contraindicated. Nonspecific measures, such as artificial fever, and particularly malarial therapy, and the use of ACTH or cortisone have yielded good results in many cases.

Differentiate orthostatic proteinuria (orthostatic albuminuria) and latent glomerulonephritis.

In orthostatic proteinuria, the albuminuria disappears when the patient is in the recumbent position for 6 hours; whereas in latent glomerulonephritis, it does not disappear and may actually increase in total amount.

Outline the prophylactic measures for the recurrence of urolithiasis.

(1) Chemical analysis of calculi, blood, and urine must be performed in order to delineate the problem.

(2) Obstructive uropathies must be eliminated.

(3) Infection must be adequately treated with a suitable antimicrobial agent or agents.

(4) A high fluid intake (3,000 to 4,000 cc. daily) must be maintained.

(5) Diet according to findings: (*a*) With calcium stones, use an acid-ash diet to make urine acid (solubility of calcium salts except oxalate enhanced in acid urine); it is desirable to maintain a pH of 5 to 6. The intake of calcium can be diminished by eliminating dairy products. (*b*) A low oxalate diet is prescribed for patients with calcium oxalate calculi. (*c*) Uric acid urolithiasis cases are given a low purine diet with sodium bicarbonate to keep the urine alkaline. Although it is impossible to lower cystine excretion by diet, the cystine may be kept in solution if the urine is kept alkaline with an alkaline ash diet.

Discuss the milk-alkali syndrome.

This syndrome is characterized by findings of hypercalcemia without hypercalciuria but with renal insufficiency and calcinosis in patients with excessive intakes of milk and absorbable alkali over long periods of time. Treatment consists in discontinuance of alkali and the administration of large amounts of fluids and chloride.

Differentiate urinary frequency and polyuria.

In any polyuric condition (diabetes, chronic glomerulonephritis, polycystic disease, etc.) increased frequency of urination occurs. However, there may be increased frequency with no change in the daily urine volume (cystitis, pyelitis, cord lesions, overflow incontinence from a distended bladder, etc.).

DISEASES OF THE BLOOD, SPLEEN, AND RETICULO-ENDOTHELIAL SYSTEM

Discuss the clinical manifestations associated with diseases of the blood.

The symptoms and signs are due primarily to the commonly associated anemia and to various changes, such as lymphadenopathy, splenomegaly, and hepatomegaly. When the hemoglobin falls to the vicinity of 11 gm. (70 per cent), the symptoms of anemia usually become apparent, and as the hemoglobin continues to fall, they become more severe. Evidences of anemia are pallor, weakness, easy fatigue, dyspnea, palpitation, headache, vertigo, fainting, and sometimes ankle edema. With a rapid loss of blood, there is evidence of shock, and with rapid destruction of blood (acute hemolytic crisis) fever and jaundice are frequently present.

Give a classification of the anemias.

In general, there is no acceptable classification of the anemias. They may be classified as to the size (M.C.V.) or hemoglobin content (M.C.C.) of the erythrocytes and as to the cause of the red blood cell loss. The first classification denotes whether an anemia is normocytic, microcytic, or macrocytic; normochromic or hypochromic. The second classification permits a subdivision as to etiology—(1) acute blood loss from hemorrhage; (2) increased destruction of erythrocytes by extrinsic causes: (*a*) sepsis (malaria, subacute bacterial endocarditis, etc.), (*b*) chemicals (lead, sulfonamide, etc.), (*c*) heat (burns), (*d*) factors concerned with immunity response (transfusions, Rh factor, etc.); or intrinsic causes: (*a*) abnormal red blood cells (sickling, congenital hemolytic jaundice, etc.), (*b*) abnormal plasma (hemolysins, cold agglutinins), (*c*) acquired hemolytic jaundice (liver cirrhosis, sarcoid, etc.); and (3) decreased production of erythrocytes: (*a*) nutritional—vitamin B_{12}, iron, folic acid and ascorbic acid deficiencies as a result of defective diet, deficient intrinsic factor (pernicious, pregnancy), intestinal impermeability (sprue, steatorrhea, etc.); (*b*) endocrine—thyroid or pituitary deficiency; (*c*) toxic—inhibition by external poisons (benzol, etc.), or internal toxins (sepsis, nephritis, etc.); (*d*) physical injury (radium, x-ray, etc.); and (*e*) mechanical interference (leukemia, metastatic carcinoma, etc.).

Discuss the characteristics of anemia due to iron deficiency.

Iron deficiency anemia in adults is usually due to chronic blood loss (also repeated pregnancies, infection); whereas in children, nutritional factors (low dietary intake or malabsorption) are of the greatest pathogenic importance. This type of anemia is characterized by the presence of hypochromic microcytic erythrocytes. Treatment consists of the detection and eradication of the source of blood loss, measures to improve the diet, or correction of intestinal disturbance, and the administration of iron.

Discuss macrocytic anemias associated with blind loop syndrome.

The common denominator in this group of macrocytic anemias is small-bowel stasis that may develop because of strictures with proximal dilatation, multiple small-bowel diverticula, or the presence of surgically produced enteric anastomoses. The most likely explanation for the anemia is competition by an abnormal intestinal flora for folic acid and vitamin B_{12}. All cases are not alike in that some show a predominant lack of folic acid, whereas others principally lack vitamin B_{12}.

Outline specific therapy for pernicious anemia (addisonism).

Vitamin B_{12} is the cornerstone in the treatment of pernicious anemia and may be employed orally or parenterally. Since absorption may be retarded when the vitamin is given by mouth, the parenteral route is preferred for most cases, especially those with combined system disease or chronic intestinal disorders. Initially, the patient is given vitamin B_{12} (15 to 30 micrograms) or its equivalent as liver injection U.S.P. intramuscularly daily for the first week, every second day for the next 10 to 14 days, and twice weekly thereafter until the blood values are normal. Subsequent therapy depends largely on the individual needs. Usually, 20 to 30 micrograms of vitamin B_{12} or its equivalent as liver injection U.S.P. intramuscularly every 2 to 4 weeks will prove adequate (no less than 1 microgram per day). In patients with combined system disease, the dosage should be doubled. Patients suitable for oral therapy should receive no less than 1 U.S.P. unit of vitamin B_{12} with intrinsic factor concentrate daily. Since some patients with pernicious anemia appear to be helped by folic acid (5 mg. daily) orally administered, it may be employed as a supplement to vitamin B_{12} but not as a substitute.

What is the significance of exercise-march hemoglobinuria?

In this condition, exercise such as walking or running in the lordotic position produces intravascular hemolysis and hemoglobinuria but exercise in the kyphotic position does not. There is no anemia, the condition is benign, the mechanism is not known, and the hemoglobinuria is not associated with myohemoglobinuria (myoglobin).

Mention five types of megaloblastic anemia other than pernicious anemia.

(1) Sprue, (2) fish tapeworm infestation, (3) pregnancy, (4) cancer of the gastrointestinal tract, (5) "achristic" anemia (idiopathic megaloblastic anemia refractory to vitamin B_{12} or liver therapy).

Describe and give treatment for the most important complication of hemophilia.

Hemarthrosis is the most important complication. It is particularly painful during the acute stages. It eventually leads to a chronic hemophilic arthritis, which often proves disabling. In addition to fresh blood or plasma transfusions, rest, ice packs, and analgesics are employed in the acute stage, whereas orthopedic management toward minimizing deformity constitutes later therapy. Aspiration of blood from a joint is contraindicated.

Give the differential diagnosis in agranulocytosis (agranulocytic angina).

Acute ulcerative tonsillitis or pharyngitis is usually accompanied by a leukocytosis. Aplastic anemia can be excluded by the absence of anemia and thrombocytopenia. Subleukemic leukemia in the early stages with severe leukopenia and oral ulceration before anemia and thrombocytopenia develop will simulate agranulocytosis, hence bone-marrow studies are required. Finally, in primary splenic neutropenia, the leukopenia is persistent and the spleen is usually enlarged. The history is of value, for in most instances the patient has been taking a drug capable of causing the disease, although occasionally no cause can be determined. It has been suggested that infection at times may be the cause rather than the result of agranulocytosis, by virtue of a process of sensitization to bacterial or viral protein.

Discuss the treatment of leukemia.

No curative method has been developed for any type of leukemia; however, therapy should be attempted in all cases because remissions obtained by judicious selection and use of available specific antileukemic therapeutic measures have been well demonstrated, especially in acute leukemias of childhood. Although adults respond less well, the subjective benefits justify therapeutic trial. In general, the therapeutic measures employed in leukemias are radiation (x-rays or radioactive phosphorus), hormones (ACTH, cortisone), and chemotherapeutic agents such as urethane, polyfunctional alkylating agents (nitrogen mustard [mechlorethamine, Mustargen]; triethylene melamine [TEM]; chlorambucil [Leukeran]), folic acid antagonists (4-aminopteroylglutamic acid [Aminopterin]; 4-amino-N^{10}-methylpteroylglutamic acid [amethopterin, Methotrexate]), and the purine antagonist (6-mercaptopurine [6-MP, Purinethol]). For the selection of the appropriate method, factors such as age of the patient, the cytological type of leukemia, its acuteness or chronicity, the degree of organ infiltration, and the state of marrow productivity must be considered. The most satisfactory therapeutic results have been obtained in acute lymphocytic leukemias and, to a lesser degree in acute granulocytic leukemia, with the antimetabolites and the hormones. Acute monocytic leukemia is occasionally helped with 6-mercaptopurine (Purinethol). X-rays and radioactive phosphorus give the best results in chronic granulocytic leukemia, although busulfan (Myeleran) and triethylene melamine (TEM) occasionally induce remission. Chronic lymphocytic leukemia is the most protracted and benign type but, on occasion, is less responsive to therapy. Irradiation has produced remissions in chronic granulocytic leukemia.

Give the treatment and common complications of polycythemia vera.

In general, treatment consists of venesection and the use of radioactive phosphorus (P^{32}). Some patients, especially young adults, without high red blood count, high total red-cell volume, and high platelet count, occasionally are controlled with infrequent venesections. However, most cases require P^{32} in addition. This is given orally or intravenously in doses of 2.5 to 5 millicuries. Subsequent therapy is dependent upon the changes in the blood picture, and a second dose, usually larger, may be required within 2 to 4 months. Leukemia and arterial or venous thrombosis are the most common complicating diseases seen with polycythemia vera. Recent reports indicate that the incidence of severe thrombotic and hemorrhagic phenomena are markedly reduced with P^{32}, and there is no evidence that P^{32} increases the incidence of leukemia.

What does the term auto-immune hemolytic disease refer to?

Certain individuals appear to have a tendency to produce abnormal globulins, one of which is a so-called "auto-antibody" that is partly responsible for accelerated red blood-cell destruction (see Coombs' test). Some of the cases are "idiopathic." Others are "symptomatic" and are associated with disorders of collagen or reticuloendothelial tissues and other diseases, such as leukemia, sarcoma, periarteritis nodosa, disseminated lupus, Hodgkin's disease, liver disease, Banti's disease, Felty's syndrome, carcinomatosis involving bone marrow, viral pneumonia, infectious mononucleosis, salmonellosis, sarcoidosis, hyperthyroidism, uremia, and porphyria erythropoietica. The treatment of both the "idiopathic" and "symptomatic" types of acquired hemolytic anemia is in general the same. ACTH and cortisone may be especially helpful in preparing selected patients for splenectomy, which is particularly beneficial in the "idiopathic" group. Blood transfusions may be advisable, although there is increased likelihood of transfusion reactions, and crossmatching is further complicated by the frequent presence of the "auto" or "pan" antibodies in the patient's serum. In addition, treatment of the "symptomatic" cases includes measures directed at the underlying disease.

Discuss the various causes of the hemorrhagic group of diseases.

In general, the hemorrhagic diseases result from vascular dysfunction, platelet deficiency, or deficient clotting mechanism. The first group includes disturbance of capillary wall integrity (toxicosis), secondary to a variety of causes—(*a*) toxic (symptomatic purpura) as in sepsis (S.B.E., meningococcemia, rickettsial diseases, etc.), (*b*) chemical agents (iodides, quinine, etc.), (*c*) chronic diseases (leukemia, nephritis, etc.), (*d*) snake venoms and fat embolism (after fractures), (*e*) anaphylactoid purpura (Schönlein-Henoch syndrome), (*f*) hypersensitivity to various allergens (bacterial, food, drugs, etc.); (*g*) vitamin C deficiency, (*h*) hereditary hemorrhagic diathesis (pseudohemophilia), and (*i*) hereditary hemorrhagic telangiectasis. The principal diseases associated with a platelet deficiency include primary or essential thrombocytopenic purpura and secondary or symptomatic thrombocytopenic purpura which is caused by a large variety of agents and diseases (drugs, chemicals, allergy, sepsis, x-rays, diseases of the blood, etc.). A deficient clotting mechanism is seen in the hemophilia group (antihemophilic globulin deficiency, plasma thromboplastic component deficiency, and plasma thromboplastic antecedent deficiency), hypoprothrombinemia (either as a result of a lack of or inadequate synthesis of vitamin K, coumarin compounds, etc.), fibrinogen deficiency (liver disease, plasma fibrinolysis), circulating anticoagulants (hemophilia-like diseases), and increased fibrinolysins (transfusion reactions, hemolytic crises).

Define and give treatment for primary splenic neutropenia.

A syndrome characterized by a profound neutropenia due to hypersequestration and hyperdestruction of granulocytes by and within the spleen, despite compensatory marrow myelopoiesis and without evidence of any related process elsewhere. Initially, the spleen is not enlarged, but it progresses in size quite rapidly; ulceration of the mouth, legs, and intestines, conjunctivitis, and cystitis are common manifestations. An epinephrine-induced contraction of the spleen is followed by a transitory increase in circulating neutrophils to a normal (or above) range. Treatment consists of splenectomy. Recovery is permanent.

What is the treatment for cirrhotic splenomegaly (Banti's syndrome)?

Treatment is directed toward the damaged liver. If treated early, further hepatic scarring and progression of the secondary hypersplenic syndrome may be prevented. In cases exhibiting a profound leukopenia or hemolytic anemia, splenectomy is indicated, despite the hazards of surgery, especially in late cases.

List the conditions included in the diagnostic category of lymphosarcoma.

Giant follicular lymphosarcoma, small-cell lymphosarcoma, leukosarcoma, and reticulum-cell sarcoma.

What findings are of diagnostic importance in multiple myeloma (plasmocytic myeloma)?

(1) By far the greatest number of patients present roentgenographically demonstrable "punched-out" osteolytic areas in the skeleton. (2) In more than 90 per cent of patients an abnormal protein can be found in the serum, the urine, or both (the use of proper electrophoresis of serum and urine can lead to the detection of multiple myeloma long before symptoms of bone pain or overt metabolic disturbances occur). Bence Jones proteinuria is demonstrable in one half of the cases. (3) The diagnosis is histologically established by bone-marrow aspiration and the demonstration of the abnormal plasma cells.

What symptoms or findings suggest the diagnosis of subleukemic (aleukemic) leukemia?

(1) Fever of unknown cause, (2) a leukopenia with a progressive anemia, (3) lymphadenopathy or splenomegaly, (4) tumefaction of gums, (5) skin lesions, (6) bone and joint pains and tenderness, and (7) a hemorrhagic tendency. The presence of any one or a combination of the above should suggest the diagnosis.

Discuss the diagnosis and various forms of Hodgkin's disease.

Regardless of the history (especially pruritus) and findings (Pel-Ebstein fever and lymph-node enlargement), the diagnosis can be established only by biopsy. In general, the disease may be classified into three forms: (1) early, strictly localized; (2) regional, in which the disease is still restricted to contiguous regions; and (3) generalized, with widespread involvement.

In what conditions may rupture of the spleen occur?

1. Trauma.
2. Leukemia.
3. Malaria.
4. Infectious mononucleosis.
5. Typhoid fever.

DISEASES OF METABOLISM AND THE ENDOCRINE SYSTEM

Discuss the etiology of diabetes mellitus.

The definite etiology of diabetes mellitus is unknown. It is true that lesions of the islands of Langerhans will give rise to hypoinsulinism, but the reasons for islet failure are not clear. Furthermore, a diabetic state can be produced by an overactive anterior pituitary, adrenal cortex, and possibly thyroid. Such other factors as heredity, diet, obesity, and diseases of the pancreas may or may not play important roles in the development of the disease.

List the complications which may occur in an inadequately controlled diabetic.

Acidosis and coma, infection (especially by staphylococcus and tubercle bacillus), arteriosclerosis (potential gangrene), peripheral neuropathy (including mental changes), ocular changes (cataracts, retinitis, glaucoma), renal damage (Kimmelstiel-Wilson syndrome), hepatomegaly, and skin involvement (local or generalized pruritus, carbuncles, xanthelasma, etc.).

What factors play important roles in the development and prognosis of diabetic acidosis and coma?

Acidosis and coma are due to disregard of dietary restrictions and insulin dosage, and/or an infectious process, gastrointestinal disturbance, or surgical complications. Prognosis in coma worsens with increasing age, presence of infection, duration and depth of coma, and previous heart and kidney disease.

What are the indications for insulin therapy?

(1) All diabetic children, (2) complications such as infections, surgery, pregnancy, and coma, and (3) inability to maintain normal weight and strength without hyperglycemia and glycosuria.

How would you diagnose a case of diabetes mellitus?

Look for diabetes in every patient, especially in obese relatives of diabetics, for often the classic symptoms—polyuria, polydipsia, pruritus vulvae, loss of strength and weight, poor resistance to infection, etc.—are not present. If the urine shows sugar, then obtain a 2-hour postprandial blood sugar and, if it is above 180 mg. per 100 cc. or above 130 mg. after fasting, diabetes is present. Should the blood sugar be below these levels, a glucose tolerance test is done. All borderline cases should be carefully checked at frequent intervals.

Outline the treatment of diabetic coma.

Diabetic coma is one of the greatest medical emergencies. Before starting therapy, it is important to get a complete history: duration of symptoms, recent insulin dosage, age, etc. Perform a careful physical examination (evidence of infection, state of hydration and consciousness, rate and depth of respirations, cardiovascular status) and test the urine for sugar and acetone (leave indwelling catheter in bladder). As a rule, the other causes of coma (alcoholism, trauma, cerebral vascular accidents, poisoning, epilepsy, meningitis, pneumonia, etc.) by this time will have been eliminated and treatment is immediately instituted. The primary aim in treatment is to restore normal feeding as soon as possible. Therapy is directed toward restoration of normal cellular and extracellular fluid ion concentrations and volumes, elimination of ketosis through restoration of normal carbohydrate metabolism, and restoration of serum pH to normal. For the most part, this is realized by giving sufficient insulin and fluid containing electrolytes. Obviously, each case is an individual problem, but in general treatment may be carried out along the following lines: (1) Draw blood for sugar, CO_2, sodium, chlorides, potassium, hematocrit, and typing and cross-matching. Culture is done where indicated. (2) Insulin—initial dose 50 units of rapid-acting insulin intravenously and 50 to 100 units subcutaneously (children require smaller doses) followed by hourly subcutaneous injection (50 to 100 units). The size of the dose will depend on rapidity of response. A useful rule, employing the qualitative Benedict test, is 20 units for 4 plus, 15 units for 3 plus, 10 units for 2 plus, and 5 units for 1 plus. (3) Parenteral fluids—at least 2,000 cc. (10 cc. per minute) of a solution containing isotonic saline (1,000 cc.), molar sodium lactate (80 cc.), and distilled water (500 cc.). (4) Start a "coma chart." (5) Keep patient warm but not hot. (6) If infection is present, administer appropriate antimicrobial agent. (7) Look for gastric distention; if present, do gastric lavage. (8) If shock is present, give plasma or blood, as well as epinephrine (0.3 to 1 cc.) or ephedrine (0.5 to 1 cc.) if the blood pressure is falling. (9) Repeat urinalysis and blood chemistry for sugar and CO_2 determinations every 4 to 6 hours. (10) Watch for signs of hypokalemia, as serum potassium and phosphorus levels fall when insulin increases the utilization of glucose. As the coma begins to yield to treatment (usually within 6 to 8 hours), glucose and potassium should be supplied. If the patient is conscious, give fruit juices, meat broth, etc.; otherwise administer intravenously (2 to 3 liters) a solution containing sodium chloride 1.8 gm., potassium chloride 1.0 gm., dextrose 20 to 100 gm., sodium lactate 2.8 gm., dibasic potassium phosphate 1.0 gm., monobasic sodium phosphate 0.14 gm., magnesium chloride 0.25 gm., distilled water for injection 1000 ml. (11) Never stop insulin. Some insulin must be given every 6 to 8 hours until the diabetic has been regulated on some form of depot insulin.

Discuss the prognosis of nondiabetic acidoses.

In general, the severity of acidosis in these cases is dependent upon the complicating disease and the state of the circulation. Acidosis resulting from starvation (including cyclic vomiting) and diarrhea can usually be handled successfully by the prompt use of solutions containing sodium, potassium, bicarbonate (or lactate), and chloride as indicated to replace fluids and electrolytes, and blood or plasma to combat circulatory collapse. Acidosis in the presence of advanced renal disease presents a much worse prognosis. Acidosis secondary to loss of pancreatic or biliary secretions by surgical drainage or fistulas or as a complication of ureterosigmoid anastomosis is readily averted.

Give the usual causes, clinical picture, and treatment of hypoglycemia in a patient receiving insulin.

For practical purposes, this reaction is the result of too little food and/or too much insulin, especially in elderly patients or "brittle" diabetics. Certain gastorintestinal disorders with vomiting and diarrhea often precipitate attacks. The symptomatology varies from mild (hunger, weakness, headache, nervous, or emotional instability) to moderately severe (sweating, tachycardia, visual disturbances, etc.), to severe (unconsciousness, convulsions, hemiplegia, etc.) manifestations. Treatment consists of the administration of glucose (oral sweets in mild cases; intravenous glucose [20 to 50 per cent] in severe reactions) and correction of the cause.

Give the differential diagnosis of insulinoma.

In a patient with a definite depression of the blood sugar level (post-absorptive below 50 mg. per 100 cc. or below 40 mg. per 100 cc. after a provocative test), the diagnosis of hyperinsulinism may be made in most instances. Whether the disease is due to a pancreatic lesion or to some other cause is of utmost importance as regards therapy. Among the other conditions causing hypoglycemia are hepatic disease, pituitary dysfunction, adrenocortical hypofunction, as well as certain functional disorders (renal glycosuria, muscular work, pregnancy and lactation, and neuroses). As a rule, the attacks in organic disease of the pancreas are more severe and of longer duration than in hyperinsulinism associated with functional disorders. Organic liver disease of sufficient severity to account for hypoglycemia may be detected by specific liver function tests (with liver disease attacks usually occur just before breakfast, in contrast to other types of hyperinsulinism in which they appear within 3 to 4 hours after eating). Disorders of the pituitary and adrenal glands can usually be suspected and substantiated, if present, by appropriate studies (x-ray of skull, Kepler's water test, epinephrine and ACTH eosinophil stimulation tests).

What is the significance of the diseases of inborn errors of metabolism?

Originally, this group of metabolic disorders was considered as innocuous, in contrast to other diseases of metabolism, such as diabetes, in that they showed no tendency towards aggravation and were not influenced by specific therapy. However, over the years, this group has been enlarged and at present contains diseases that may become aggravated with age and some in which therapy may favorably influence the course. Included among the inborn errors of metabolism are such diseases as gout, the glycogen storage disorders, sicklemia and other hemoglobin anomalies responsible for hemolytic anemia, Wilson's disease, some of the lipoidoses and essential hypercholesterolemias, familial periodic paralysis, some of the progressive muscular dystrophies and myotonias, albinism, alkaptonuria, pentosuria, aminoaciduria, porphyuria, etc. As indicated, most of these are relatively rare diseases and are of limited practical importance, but as a result of their study, problems related to intermediary metabolism have become more clarified, especially those pertaining to the identification of enzyme deficiencies and the relation of genes to the chemical and enzymatic constitution of cells.

Outline the treatment of gout.

Although gout is not curable, control of the disease with the now available measures can be highly successful. During the acute stage, the treatment of choice is colchicine and/or ACTH gel. Colchicine is given by mouth 0.5 mg. at hourly intervals for 6 to 8 doses, depending on the development of gastrointestinal symptoms. This may be repeated in 48 hours, if necessary. ACTH gel intramuscularly, 100 units, often seems miraculous in that symptoms often subside within 12 to 24 hours. If necessary, ACTH gel, 50 units, may be repeated in 36 to 48 hours. When employing this method, it is best to administer colchicine, 0.5 mg. by mouth 3 times daily and continue for 7 to 10 days to prevent relapse. Phenylbutazone (Butazolidin) is also used effectively, 400 to 600 mg. daily in 4 divided doses by mouth, or intramuscularly 1.0 gm. daily for 2 to 3 days. In cases with single joint or bursal involvement, the aspiration of fluid, followed by the instillation of hydrocortisone (Hydrocortone, Cortef) 25 mg. is usually highly successful. For the most part, gout will recur with varying degrees of frequency. In infrequent, mild cases, a diet that eliminates high purine foods (kidney, liver, sweetbreads, stews, gravy, broth, bouillon, sardines, roe, etc.) and alcohol is advisable. If the serum uric acid is elevated and/or the attacks occur at frequent intervals, probenecid (Benemid) 0.5 mg. twice daily in combination with colchicine 0.5 mg. daily represents a satisfactory regimen. Probenecid or colchicine alone has been observed to control gout in some instances.

What is the cause of obesity?

Obesity is usually considered to be of two types—exogenous (over-supply of food) and endogenous (increased caloric intake because of disturbances within the body). Although certain endogenous factors, such as endocrine disturbances (thyroid, gonads, pituitary, etc.), are often accompanied by overweight, the fact remains that the excessive intake of calories is the only cause of obesity. A person who is not ambulatory and cannot exercise will often gain weight as a result of a normal intake of food which, under the circumstances, is excessive. Frequently a psychoneurotic will use overeating as a substitute for unsatisfied desires or obesity as a defensive or offensive weapon.

Discuss the treatment of atherosclerosis.

Since the exact etiology of this disease remains obscure, treatment is for the most part directed at conditions frequently associated with it (obesity, hypertension), abnormal chemical composition of the plasma (cholesterol, etc.) and to the accidents dependent upon the changes in the blood vessels (cerebral, coronary, peripheral arteries, etc.). In general, it seems advisable to employ a low caloric diet containing unhydrogenated vegetable fat but no animal fat, in that it will often reduce the serum lipids as well as the body weight. Various preparations containing choline, methionine, lipocaic, etc. have been tried, but their effectiveness has not been established. In addition, the use of anticoagulants in the prevention of serious complications in coronary thrombosis and possibly in thrombosis elsewhere is of value. Finally, the employment of hypotensive agents in cases with hypertension is likewise beneficial.

Give the diagnosis of secondary amyloidosis.

Clinically, this disorder is suspected in any patient suffering with a suppurating disease, especially in those with marked albuminuria or the nephrotic syndrome. Biopsy of gingival tissue, liver, kidney, and suspicious skin and muscle areas may secure the diagnosis. Because of inconclusive results and frequent untoward reactions, the Congo red test is rarely used as a diagnostic procedure.

Discuss the etiology of osteoporosis.

In this disease, the primary disorder is a failure to produce bone matrix, as a result of either deficient osteoblastic activity or inadequate amounts of essential nitrogenous components of which the matrix is composed. Since bone matrix is composed in part of nitrogenous tissues, osteoporosis represents a disorder of protein, rather than of calcium and phosphorus metabolism. Furthermore, in this disease, there is no failure of the matrix to calcify, as in osteomalacia, nor is there increased bone destruction, as in osteitis fibrosa cystica. In conditions in which there is a diminution or cessation of essential stimuli to osteoblastic activity, osteoporosis may appear. The most common example is the postmenopausal form, which results from a lack of estrogenic hormones that stimulate osteoblastic activity. Likewise, the normal strains on the skeleton provide an essential stimulus to osteoblastic activity, and their diminution by immobilization leads to disuse atrophy of the bone. Osteoporosis due to defective matrix formation may occur when the essential nitrogenous materials are inadequate (malnutrition) or are diverted toward caloric requirements (hyperthyroidism, diabetes), or as a result of conditions causing catabolism of protein tissues, such as the "carbohydrate active" steroids of the adrenal cortex (prolonged treatment with ACTH, cortisone, and related steroids, the "alarm reaction," Cushing's syndrome). In addition, osteoporosis may occur in eunuchoid and possibly in senile males as a result of a lack of androgen steroids, which have the property of producing anabolism of protein tissues. Finally, there is a group of so-called "idiopathic" osteoporoses for which no definite mechanism of development is known.

Mention the common diseases of the pituitary gland.

(1) Tumors originating in the hypophysis that produce their effect by producing an overabundance of hormone (acidophilic—gigantism, acromegaly; basophilic—Cushing's syndrome) or by reducing the amount of hormone formed in one of the other types of cells through pressure (chromophobe-cell tumor); (2) hypofunction as a result of atrophy or destruction of the gland (dwarfism, panhypopituitarism, diabetes insipidus).

Outline the clinical manifestations and findings of panhypopituitarism (Simmond's disease).

This disease is due to destruction of the anterior lobe of the pituitary gland by embolism, abscesses, hemorrhage, gumma, tuberculosis, or by tumor of or near the gland. It is seen frequently after severe postpartum hemorrhage. Clinically, the condition is manifested by (although not all present in a given patient): weakness; weight loss; loss of hair with premature graying; dryness, pallor, and atrophy of skin; loss of sex function; loss of teeth; low body temperature; hypotension; apathy and depression; low basal metabolism; hypoglycemia; very low or absent excretion of 17-ketosteroids and corticosteroids; and high cholesterol.

Give etiology, clinical manifestations, and treatment of Cushing's syndrome.

This condition is caused by an excessive production of 11-oxysteroids (hydrocortisone and corticosterone) as a result of adrenal hyperfunction due to hyperplasia, adenoma, or carcinoma of the adrenal cortex, or as a result of a basophilic adenoma in the anterior pituitary, secreting excess adrenocorticotropic hormone, thus over-stimulating the adrenal gland. The manifestations of the fully developed syndrome may include obesity (buffalo type), atrophy of skin, purple striae of the trunk, hirsutism, muscular weakness, amenorrhea, diabetes mellitus, hypertension, and osteoporosis. Treatment consists of surgical removal of the tumor or hyperplastic gland (only 10 per cent of tissue left). Patients with mild Cushing's syndrome may be given a trial of conservative therapy—x-ray treatment to the pituitary to control excessive ACTH production and testosterone propionate, 25 mg. intramuscularly daily, to promote protein anabolism and to inhibit the production of corticosteroids.

Discuss the diagnosis of hyperthyroidism.

The diagnosis should be readily apparent in the presence of its typical features—goiter, exophthalmos, tumor, and tachycardia. At times, the diagnosis is more difficult when the disease masquerades as refractory heart failure, atrial fibrillation, insulin-resistant diabetes, chronic diarrhea, etc. Furthermore, significant hypermetabolism occurs in the absence of thyroid dysfunction—notably, in lymphoma and other malignancies, acromegaly, pheochromocytoma, adrenal cortical hyperplasia, etc. Likewise, anxiety states may simulate hyperthyroidism, although the true hypermetabolic features (resting tachycardia, hot moist hands, good tolerance for cold, and weight loss associated with an excessive appetite) are most unusual in the unstable, anxious, asthenic individual. Although the diagnosis of hyperthyroidism is based primarily on clinical observations, this suspicion must be supported by selected laboratory studies. (See page 211.) On occasion, when the diagnosis is questionable, one may resort to a therapeutic test, preferably with propylthiouracil over a 3-month period.

Outline the treatment of hypothyroidism.

The most effective treatment of hypothyroid states is the use of a good desiccated thyroid substance. In cretinism, an early diagnosis is important because, if treatment is begun too late, growth cannot be promoted to a sufficient degree nor can mental retardation be reversed. The results in myxedema are usually good and there is definite improvement within 2 months' time. The amount of thyroid substance required varies with the individual case; the effect of therapy is gauged and the dose is regulated by watching the basal metabolic rate, cholesterol concentration, the pulse rate, and the disappearance of clinical signs of the disease. Most cases respond to relatively small doses (0.015 to 0.030 gm.) daily for 14 days and then increase to 0.06 gm. to 0.12 gm. daily. A maintenance dose of 0.1 gm., or more, daily is required in most patients for life.

Give the clinical picture of acute thyroiditis.

This condition usually follows an infection, such as tonsillitis, pneumonia, typhoid fever, etc., and is characterized clinically by chills, fever, tachycardia, dysphagia, and pain in the thyroid region, neck, shoulders, and arms. The leukocyte count and blood sedimentation rate are increased, the basal metabolic rate may be normal or elevated, the protein bound iodine is normal or high, and the I^{131} uptake is low.

Discuss the relationship of the thymus gland to myasthenia gravis.

For the most part, little is known concerning the function of the thymus gland, although in over half of the reported autopsies of cases of myasthenia gravis some abnormality of the thymus has been noted. However, thymectomy for myasthenia gravis has not exerted a definite beneficial effect.

List the causes, clinical findings, and treatment of hyperparathyroidism.

Primary hyperparathyroidism is due to an excessive production of parathyroid hormone resulting in mobilization of calcium phosphate from the skeleton and increased renal excretion of phosphorus. This may be caused by a single or multiple hyperfunctioning adenoma, parathyroid carcinoma, or by diffuse hypertrophy and hyperplasia of all four parathyroid glands. Clinically, this disease is suggested by a combination of renal calculi, generalized osteitis fibrosa cystica, hypercalcemia, and hypophosphatemia. The treatment is surgical. Secondary hyperparathyroidism results from conditions such as faulty intestinal absorption (sprue) or retention of phosphates (renal insufficiency). The treatment is that of the underlying disease.

What symptoms and findings are suggestive of pheochromocytoma?

Excessive sweating, an elevated basal metabolic rate, and hypertension; paroxysms of palpitation, headache, hypertension; all patients with a sustained hypertension, glycosuria, hyperglycemia. A patient who has any or all of the above should be suspected of having a pheochromocytoma.

List the symptoms and signs of chronic adrenal insufficiency (Addison's disease).

The course of this disease is insidious and progressive and is interrupted by exacerbations, crises, and remissions over the course of several years. The exacerbations are provoked by infections, trauma, and undue exercise. The chief complaint is that of asthenia, and loss of weight is common. Practically all patients show pigmentation. Nervousness, insomnia, loss of appetite, nausea, vomiting, and abdominal pain are frequently present. The blood pressure is characteristically low. Salt-craving, when present, is a very suggestive symptom.

What is eunuchism?

A eunuch is a male with complete loss of testicular function as a result of castration, malignancy, inflammation, or injury. If this occurs before sex maturation takes place, secondary sex characteristics fail to appear, and there is a complete absence of sexual instinct. If it occurs soon after puberty, there is some regression of the secondary sex characteristics. If it occurs late, after sex characteristics are well established, there is very little change in the body configuration and little loss of libido.

Discuss and give treatment of cryptorchism (undescended testes).

True cryptorchism may be due to a mechanical factor preventing one or both testes from descending into the scrotum, or to an endocrine disturbance —insufficient testicular hormone secretion—which in turn may be due to a failure of the anterior lobe to secrete a sufficient amount of gonadotropic hormone. The importance of this condition lies in the fact that the testes cannot function normally except in the environment of the scrotum. Before starting any form of therapy, it is important to distinguish true cryptorchism from pseudocryptorchism in which the testes are migratory and move back and forth spontaneously from the scrotum to a higher level. Migratory testes require no treatment, for they tend to remain in the scrotum after puberty. Treatment of true cryptorchism consists of a combination of glandular and surgical procedures. In a certain number of cases, the testes can be made to descend by the injection of repeated doses of chorionic gonadotropin, 1,300 to 1,000 units weekly for 1 to 2 months. If this form of therapy fails, surgery is indicated, since some mechanical factor is often responsible.

Define primary aldosteronism.

This syndrome results from overproduction of aldosterone (electrocortin), an extremely potent sodium-retaining corticoid, and consists of periodic severe muscular weakness, intermittent tetany, and paresthesia, polyuria, polydipsia, hypertension but no edema, and certain characteristic biochemical changes in the blood—hypokalemia, hypernatremia, and alkalosis. This condition originates in the adrenal gland, in contrast to so-called secondary aldosteronism (edematous nephritis, congestive heart failure, decompensated hepatic cirrhosis, and eclampsia), in which excessive amounts of aldosterone are found in the urine. It is assumed that in the latter instances a metabolic event occurs which is common to them and which triggers the production of excessive amounts of this sodium-retaining steroid. Patients presenting the clinical and laboratory manifestations of primary aldosteronism should be treated surgically.

Give the etiology of Löffler's syndrome (allergic pneumonia).

This condition consists essentially of transitory pulmonary infiltrations associated with a blood eosinophilia. It is thought to be an allergic response in most instances. Among the allergens identified have been various intestinal parasites, pollens, sulfonamides, and penicillin.

What effects do large amounts of androgen produce in females?

(1) Suppression of ovarian function, which is due primarily to suppression of pituitary gonadrotropic function, with atrophy of uterus, vagina, and often the breasts; (2) virilization, with enlargement of the clitoris, growth of facial and body hair, deepening of the voice, etc.

Discuss the etiology of gynecomastia.

Gynecomastia, an enlargement of the breast tissue of males, may be caused by an endocrine disturbance, particularly an increase of estrogenic substances. Testicular tumors, other tumors, and adrenal cortical hyperplasia may be associated with this condition. Hepatic disease (cirrhosis) and dietary deficiency also may bring about gynecomastia.

Explain the increase in free estrogen content in the urine of patients with hepatic disease.

Patients with hepatic functional impairment (particularly cirrhosis) often exhibit clinical manifestations of hyperestrogenism, such as menstrual disorders in the female and gynecomastic and testicular atrophy in the male. In these cases, the estrogen content of the urine is often increased, and there is some evidence that this is due primarily to protein and vitamin B deficiency which interferes with hepatic inactivation of estrogens.

Discuss endocrine allergy.

Since some hormone preparations are proteins and many others contain traces of protein substances, it is not surprising that a number of true allergic reactions have been reported after their administration. For example, (1) the hormone itself may be responsible, as insulin, corticotropin (ACTH), and pancreatic enzymes (Tryptar, Dornovac); (2) the vehicle or menstruum may be the sensitizing agent, e.g., oils of corn, peanut, or sesame; (3) since some hormone preparations are derived from animal sources, reactions to beef and pork are possible; and (4) the possibility of a person's becoming sensitive to his own hormones must be considered: thyroid allergy is an example of an auto-immune mechanism.

DISEASES OF THE LOCOMOTOR AND NERVOUS SYSTEMS

Differentiate between arthritis and rheumatism.

Arthritis may be defined as any inflammatory condition in a joint, although in certain types of joint diseases inflammation is not a striking feature, but rather there are occasional aches and stiffness, followed by crippling. The term "rheumatism" has a broader connotation. It is frequently applied to a large group of diseases of the musculoskeletal system that affect joints, muscles, tendons, and other related structures and are characterized by pain and stiffness.

Symptoms referable to articular structures may be caused by a variety of etiological agents. The most convenient working classification of diseases of the joints is shown in the following outline, recommended by The American Rheumatism Association:

(1) Arthritis due to specific infection. Specify organism when known.
(2) Arthritis due to rheumatic fever.
(3) Arthritis, rheumatoid. Specify as multiple or of spine.
(4) Degenerative joint disease, multiple due to unknown cause; osteoarthritis.
(5) Arthritis due to direct trauma.
(6) Arthritis due to gout.
(7) Neurogenic arthropathy.
(8) New growths of joints.
(9) Hydrarthrosis, intermittent.
(10) Periarticular fibrositis.
(11) Myositis, bursitis, neuritis, and neuralgia.
(12) Diseases in which arthritis, arthropathy, or arthralgia are frequently associated (diagnose disease, list joint manifestation as symptom):

Acromegaly
Acute disseminated lupus erythematosus
Cyst of meniscus of knee
Dermatomyositis
Drug intoxication (specify)
Erythema multiforme exudativum
Erythema nodosum
Hemophilia
Hysteria
Ochronosis
Osteochondritis dissecans
Osteochondromatosis
Periarteritis nodosa
Psoriasis
Pulmonary osteoarthropathy
Purpura, various types
Raynaud's disease
Reiter's disease
Scleroderma
Serum sickness

Give the fundamentals concerned with the management of arthritis.

The successful treatment of an arthritic patient is one of the real challenges in the practice of medicine. For the most part, the patient is a victim of some chronic disease and marked improvement usually results only after months, or even years, of close observation and care of the patient. An optimistic attitude, both by the patient and physician, is the cornerstone of success in such cases. Every effort should be made to classify the type of arthritis, its cause, and precipitative factors. This information aids greatly in the intelligent use of the various therapeutic tools—psychotherapy, physical therapy, chemotherapy, dietotherapy, hormonal agents, etc.

Give the differential diagnosis of rheumatoid arthritis (atrophic or chronic proliferative arthritis, arthritis deformans).

The diagnosis is usually apparent in a patient presenting the classic features: prodromal symptoms (fatigue, lassitude, loss of appetite and weight, etc.), paraesthesias, symmetric involvement of joints with fusiform swelling of fingers, remissions, and relapses. However, the diagnosis is more difficult when the disease has an abrupt febrile onset, is migratory, has asymmetrical or monoarticular joint involvement, skin rash, etc. Among the diseases most likely to be confused with rheumatoid arthritis are:

(1) Rheumatic fever, particularly in children: Usually a freedom of joint involvement between attacks, prompt and permanent relief with salicylates, development of murmurs and electrocardiographic changes, and an elevated antistreptolysin O titer all help in distinguishing this disease.

(2) Gout, at times, will assume an acute polyarticular form, but a history of periodicity, complete relief between attacks, frequent involvement of the great toe, response to colchicine, and an elevated serum uric acid should not offer too much difficulty in diagnosis.

(3) Gonorrheal arthritis can usually be ruled out by the history, examination of the genitourinary tract, isolation of gonococci from infected foci, changing titer of complement-fixation test, and response to penicillin therapy.

(4) Disseminated lupus erythematosus in the early stages may be confused with rheumatoid arthritis, but the later manifestations with involvement of the skin, pleura, lungs, etc., and the demonstration of L. E. cells are helpful in establishing the diagnosis.

In addition, many other conditions accompanied by migratory joint pains may be confused with rheumatoid arthritis. Degenerative (hypertrophic) arthritis does not usually present a serious diagnostic problem, although one should remember that rheumatoid arthritis may be superimposed on a degenerative process. It is important to differentiate between rheumatoid and degenerative arthritis because the treatment is quite different for the two.

Differential Diagnosis of Rheumatoid Arthritis (Cecil)

	RHEUMATOID ARTHRITIS	DEGENERATIVE ARTHRITIS
Average age of onset	Third and fourth decades	Fifth and sixth decades
Weight	Normal or underweight	Usually overweight
Condition of bones	Osteoporosis	Condensation of articular margins
Joints involved	Any joint in body	Chiefly knees, spine, and fingers
Type	Migratory	Not migratory
Appearance of joints	Periarticular swelling	No swelling
Special signs	Fusiform finger joints	Heberden's nodes
Subcutaneous nodules	Present in 10 per cent of cases	Never present
Roentgen ray	Narrowing and clouding of joint space	Lipping of bony margins of joint
Joint fluid	Turbid. Increased cells and protein	Clear. Few cells. Low protein

Differential Diagnosis of Rheumatoid Arthritis (Cecil)—(Cont.)

	RHEUMATOID ARTHRITIS	DEGENERATIVE ARTHRITIS
Streptococcal or sheep-cell agglutinins	Usually present	Never present
Blood count	Secondary anemia and slight leukocytosis	Normal blood count
Sedimentation of RBC	Considerably accelerated	Normal or slightly accelerated
Course	Usually progressive	Stationary or slightly progressive
Termination	Ankylosis and deformity	No ankylosis; usually no deformity

Outline the treatment of rheumatoid arthritis.

Rest and Relief of Pain: In general, the severity of the constitutional symptoms, activity of the inflammatory process, or involvement of weight-bearing joints determines whether bed rest is necessary. The relief of pain is important if the patient is to obtain proper rest, as well as to permit the regular use of exercise to maintain joint function. The salicylates are the most satisfactory agents for relief of pain and stiffness and should be administered regularly (50 to 100 grains daily, in divided doses). Small doses of barbiturates, in addition, are frequently of value in certain patients. Phenylbutazone (Butazolidin), 100 mg. four times daily, may be used in patients unable to take, or not helped by, salicylates.

Physical Therapy: By means of special exercises and local heat (infrared lamps, bakes, contrast and paraffin baths). This plays an important role in preserving and improving joint function and relieving pain. In addition, pillows, splints, or molds, and corrective orthopedic measures are employed where necessary.

General Measures: These include an adequate caloric diet, high in proteins, supplemented with vitamins, particularly ascorbic acid and members of the B complex group. Iron (ferrous sulfate 0.3 gm. three times daily) for anemia and blood transfusions should be given, if indicated. In the presence of endocrine deficiency, the appropriate substance is employed.

Additional Therapeutic Measures: In patients who do not respond satisfactorily to conservative measures or in whom the disease is severe, additional forms of therapy are indicated:

(*a*) ACTH, CORTISONE, AND RELATED STEROIDS: These agents are capable of suppressing most of the manifestations of the disease but are not curative. For the most part, their suppressive effect is associated with some degree of hyperadrenalism, which, if prolonged, may result in certain undesirable consequences. Therefore, these agents are used only with patients in whom their use can be limited to a period not exceeding four months, for the control of severe flare-ups, and in those individuals who obtain noticeable relief on relatively small doses, which result in only slight manifestations of hyperadrenalism. For the most part, ACTH (corticotropin), since it must be injected intramuscularly (40 to 60 mg. daily), is not used for long-term therapy, but rather to restore adrenal responsiveness in patients who have been receiving adrenocortical steroids, or in initial steroid therapy when an unusually prompt effect is desired and it is important to avoid the complicating factor of adrenal suppression. Some workers recommend alternating courses of ACTH and cortisone in the treatment of rheumatoid arthritis. In general, the effects of cortisone acetate (Cortogen Acetate, etc.) and the newer adrenal glucocorticoids are the same and may be discussed as a group (see commonly employed adrenal glucocorticoids, page 193). Treatment is initiated with 80 mg. daily, in 3 to 4 divided doses, for a period of 4 to 7 days, and then the dosage is reduced gradually because the beneficial results may be lost by an abrupt cessation of medication. The dose is reduced every 7 to 10 days, in decrements not exceeding 15 mg. of cortisone (other steroids in proportion) until the maintenance dose of 50 mg. daily is attained. Hydrocortisone acetate (Cortef Acetate, Cortril Acetate or one of the newer preparations) injected locally into the joints, may be useful for patients in whom one or two joints show persistent active synovitis, in spite of improvement in other joints. The usual dosage is 25 mg., which may be repeated as the effect wears off (which may vary from a few days to several weeks). It is important that the injections be carried out with strict sterile precautions, preferably not in a hospital (resistant organisms).

(*b*) GOLD SALTS: With the advent of ACTH and cortisone, there has been less enthusiasm for the use of gold preparations in the treatment of rheumatoid arthritis. In fact, some authorities, because of the toxic reactions and because of the high percentage of relapses, question the advisability of chrysotherapy. Nevertheless, other workers endorse the use of gold, in spite of its drawbacks. Gold thioglycose (Solganal B) and gold sodium thiomalate (Myocrisine) are the most commonly employed gold preparations. The usual dose (intramuscularly) is 10 mg. initially, followed in one week by 25 mg. and then 50 mg. weekly for 22 weeks. After a rest period of four to eight weeks, 50 mg. is given every two to three weeks for an indefinite period. Precautionary measures are important as regards gold toxicity. Pre-existing liver and kidney diseases are definite contraindications to its use. During therapy, the patient should be observed at weekly intervals for evidence of dermatitis, stomatitis, renal or hepatic damage, or bone-marrow depression. If toxicity develops, the gold should be stopped, and, if it is severe, dimercaprol (BAL) should be used. The skin manifestations are frequently controlled with ACTH.

Foci of Infection: Although the theory that rheumatoid arthritis is caused by focal infection has been largely discredited, every effort should be made to detect and eradicate possible foci of infection. At times this proves helpful.

Give the clinical manifestations and treatment of Reiter's syndrome.

This disease, of unknown etiology, is characterized by the classic triad of urethritis, conjunctivitis, and polyarthritis, that usually follow each other in that order, taking from 2 to 40 days for the syndrome to manifest itself. Usually, a low grade fever is present and diarrhea may precede or accompany the disease. The urethritis varies from a slight serous discharge to a profuse purulent one and is usually of short duration. Conjunctivitis is often bilateral and accompanied by abundant pus and may be followed by keratitis or iritis. Arthritis is usually polyarticular and involves chiefly the weight-bearing joints, which occasionally may be permanently injured. The disease tends to run in cycles with one or more recurrences. Treatment should be undertaken as described for patients with rheumatoid arthritis. Favorable results have been obtained with streptomycin or tetracycline; these are worthy of trial. ACTH and cortisone have also been used successfully, especially in overcoming the acute inflammatory disease of the eyes and joints and in permitting earlier and more active physical therapy.

Define infectious polyneuritis (Landry-Guillain-Barré syndrome).

Infectious polyneuritis is a clinical syndrome of unknown etiology characterized by the acute onset of symptoms of involvement of the peripheral and cranial nerves. A history of a preceding infection of the upper respiratory or gastrointestinal tract is obtained from about two thirds of the patients. Aside from the neurological changes, the most common finding is an increase in the cerebrospinal fluid protein, with values as high as 1000 mg. per 100 cc. in some cases. The protein is not always increased, however, and, when present, is usually found in the early stages; occasionally, however, the protein content of the fluid may be normal in the early stages and increased in the later stages.

What is the fibrositis syndrome?

For many years, the term "fibrositis" was used for inflammatory changes in fibrous tissue throughout the body that resulted from local or general infection or trauma and gave rise to pain, aching, and stiffness. Subsequent histological studies, however, have failed to confirm the presence of chronic inflammation, and today fibrositis remains a controversial condition. Hence, the term "fibrositis syndrome" has been coined to designate a well-recognized symptom complex, rather than a disease entity, which is brought on by a variety of widely separate factors, such as trauma, exposure, infection, fatigue, or vascular, metabolic, occupational, and psychogenic conditions. The outstanding symptoms are pain, aching, and stiffness, particularly of the neck, shoulder, lower back, and chest; easy fatigue; and unusual tiredness, especially after a night's rest. Physical examination is essentially negative, except for a localized tender area, or myalgic spot, the so-called "trigger point" of fibrositis, and perhaps some limitation of movement.

What complications may be associated with osteitis deformans (Paget's disease of bone)?

(1) Extensive deformity and crippling with progression of disease; (2) arteriosclerosis, more advanced in this disease than usually seen; (3) deafness; (4) nephrolithiasis; (5) cardiac hypertrophy and congestive failure resulting from increased blood flow to involved bones (i.e., arteriovenous-like mechanism); (6) osteogenic sarcoma, the incidence of which after age 40 is more frequent in patients suffering with osteitis deformans.

Differentiate between the childhood and facioscapulohumeral types of progressive muscular dystrophy.

Childhood Type: Begins in early childhood, usually affects males, is frequently inherited as a sex-linked recessive mendelian trait, involves the muscles of the trunk and pelvis initially, is often accompanied by pseudohypertrophy of the muscles (especially the calves), is rapidly progressive, with contractures of the muscles leading to complete disability that is seldom compatible with survival to adult life.

Facioscapulohumeral Type: Appears in late childhood or in adolescence, is characteristically inherited as a mendelian dominant, affects both sexes, involves the facial and pectoral-girdle muscles early, and is rarely accompanied by muscular enlargement. As a rule, only a few patients are totally incapacitated.

What are the common causes of extracranial headaches?

Most extracranial headaches are the result of painful dilatation, distention, and edema of cranial arteries (vascular headache—migraine, arterial hypertension, Ménière's disease, "occipital neuralgia," etc.); and sustained contraction of skeletal muscle about the face, scalp, neck (muscle-contraction headache—emotional tension, myofibrositis, arthritis, etc.). Less frequently, extracranial headaches are caused by acute or chronic disease of the eye, ear, nose, teeth, and paranasal sinuses, or are due to nonspecific inflammation of cranial arteries ("temporal arteritis," etc.).

Define the post-traumatic syndrome.

A symptom complex of headache, dizziness, difficulty in concentration, and often nervous instability which follows a head injury. The pathogenesis of this condition is not clear in that some ascribe it to organic damage to the brain, while others would put the syndrome more definitely on a psychogenic basis. For example, the symptoms are more likely to occur and become chronic in a person whose nervous temperament predisposes him to such responses. Likewise, the severity and duration of symptoms are influenced by domestic and financial difficulties and whether or not compensation claims remain unsettled. In some instances the patient is fearful of permanent brain injury. This syndrome, especially in the early stages, is to be differentiated from post-traumatic subdural hematomas, which may produce the same symptoms, but the focal signs, changes of consciousness, and progression of symptoms and signs set it apart from the post-traumatic syndrome.

Give the symptoms, management and prevention of migraine headache.

Periodic headache, usually unilateral, which may vary in severity but is often characterized as a severe stabbing, throbbing, or aching pain that may last a few hours to several days. The headache is associated with "irritability," nausea, and often photophobia, vomiting, diarrhea, or constipation. Preheadache phenomena include dizziness, visual disturbances, and paraesthesias, which may occur several hours to several days preceding the headache. Mild attacks are usually controlled by rest in a dark room, mild sedation, and acetylsalicylic acid or codeine phosphate. For severe episodes, ergot is the best form of therapy. Intramuscular injection of ergotamine tartrate (Gynergin), 0.25 mg. to 0.5 mg., will usually give relief, especially if administered within an hour of the onset of the attack. Although less effective, ergotamine tartrate may also be given by mouth, 5 mg., followed by 2 mg. every half hour until the headache is relieved or until a maximum total dosage of 11 mg. has been taken. In patients in whom the use of ergotamine tartrate is regularly accompanied by nausea and vomiting, the intravenous administration of dihydroergotamine (1 mg.) is preferable, in that this latter preparation is less toxic and may be the drug of choice for parenteral use of ergot. Numerous therapeutic procedures have been tried for preventing or decreasing the frequency of migraine attacks, but none is specific or universally effective. However, certain measures are worthy of trial. The most important single factor is psychotherapy directed toward relief of anxiety and the improvement of personality or situational difficulties. The patient should avoid undue fatigue, particularly eyestrain. Normal bowel function and regularity in sleeping habits should be maintained. In addition, any element in diet, such as specific food sensitivity, or anything in the environment with which the patient comes in contact that might be a specific agent in causing attacks of migraine should be watched.

Outline the treatment of histamine headaches.

Horton has called attention to a group of patients presenting a syndrome characterized by unilateral head pain of extreme severity but of relatively brief duration; this is accompanied by homolateral conjunctival congestion and lacrimation, rhinorrhea, nasal obstruction, and increased perspiration. The pain occurs in the distribution of the external carotid artery, which is often very sensitive to pressure. He found that a typical attack could be produced by the subcutaneous injection of 0.35 mg. of histamine base (1.0 mg. of histamine phosphate). Epinephrine hydrochloride solution (1:400,000) intravenously stops the spontaneous or induced attacks promptly.

He reported that these patients could be "desensitized" to histamine and recommended the following regimen. Prepare a solution of histamine phosphate containing 0.275 mg. per ml. Subcutaneous injections are given twice daily in these doses: 0.10 ml.; 0.15; 0.20; 0.25; 0.30; 0.35; 0.40; 0.45; 0.50. If the patient has not been relieved it is advisable to continue the injections, increasing the dose in the same manner, to 1.0 ml. If the patient notices flushing of the face or other symptoms after any injection, the next dose should be one half of the amount that caused the reaction, and the size of subsequent doses should be increased very slowly.

What conditions predispose cerebral hemorrhage? What parts of the brain are most liable to hemorrhage?

Aneurysms, congenital and acquired; arteriosclerosis; hypertension; syphilis; vitamin deficiency; infections; brain tumor; blood dyscrasias.

The parts supplied by the middle cerebral artery.

Discuss the use of anticoagulants in the treatment of cerebral vascular accidents.

Anticoagulants are administered to patients with embolic or thrombotic lesions with the aim of preventing the development of new lesions. It would seem that these agents are indicated in patients with a history of recurrent cerebral emboli secondary to rheumatic or other forms of heart disease and in patients with recurrent vascular symptoms, presumably due to intermittent insufficiency of the carotid or basilar circulation. The anticoagulants are contraindicated in patients with an intracerebral hemorrhage or a total occlusion of a branch of one of the major vessels. At the present time there are no established criteria for the length of period of anticoagulant therapy.

Give the symptoms and signs of occlusion of the posterior inferior cerebellar artery.

Dysphagia and weakness of the homolateral half of the palate, caused by destruction of the nucleus ambiguus; loss of taste on the homolateral side of the tongue, resulting from damage of the solitary fasciculus; impairment of the appreciation of pain and temperature in the homolateral side of the face, as a result of dysfunction of the descending root and spinal nucleus of the trigeminus; Horner's syndrome in the homolateral eye, which is due to loss of the descending sympathetic fibers; nystagmus, owing to damage of the vestibular nuclei; cerebellar dysfunction in the homolateral arm and leg, caused by necrosis of the restiform body and cerebellum; and impaired recognition of pain and temperature stimuli on the opposite half of the body due to destruction of the medullary part of the lateral spinothalamic tract.

What are the causes and symptoms of abscess of the brain?

The *causes* are traumatism; mastoid disease following otitis media; abscess elsewhere in the body, as in the lungs or liver; ulcerative endocarditis; etc.

The *course* may be acute, with high fever, rigors, headache, delirium, convulsions, vomiting, and coma. The general *symptoms* in chronic cases are headache, mental impairment, vertigo, vomiting, irregular fever, stupor, and loss of flesh and strength. The focal phenomena vary with the site of the abscess.

Give the clinical picture of cavernous sinus thrombosis.

Homolateral frontal headache and facial pain, followed by proptosis, edema of eyelids, chemosis of conjunctivae, and paresis of oculomotor nerves.

What specific tests are commonly employed in the diagnosis of an intracranial tumor?

(1) X-rays of the skull may show displacement of the pineal gland (indicative of an expanding lesion); increase in digital markings on the vault and erosion of the clinoid process of the sella turcica (characteristic of increased intracranial pressure); and localized erosion or overgrowth of the skull, increased vascularity, and areas of calcification and ballooning of the sella turcica (common findings in the presence of a tumor). (2) Cerebrospinal fluid examination may show an increase in protein content, as well as an increased spinal

fluid pressure. Both of these findings are associated with brain tumor. (3) Air injection into the lumbar subarachnoid spaces (encephalography) or, if the intracranial pressure is increased, air injected into the ventricles (ventriculography), followed by x-rays of the skull, will demonstrate the presence of a tumor mass by changes in the size and shape of the ventricles and subarachnoid cisterns. (4) Cerebral angiography is employed to detect vascular abnormalities resulting from pressure from an avascular neoplasm or from the vascularity of the tumor. (5) Electroencephalography may reveal abnormalities that indicate the presence of a focal lesion and thus be of value in localizing the tumor.

Differentiate the coma of opium poisoning from that of cerebral hemorrhage.

APOPLECTIC COMA

Deep coma; sudden onset. If any injury, only a scalp wound.
Pupils unequal or dilated. Contracted in hemorrhage into the pons.
Pulse full and slow.
Respiration slow and stertorous.
Temperature higher on paralyzed side, but lower in rectum.
Urine contains trace of albumin.
Hemiplegia with convulsions on one side.

OPIUM POISONING

Can be aroused unless coma is very deep.
Pupils contracted to pinpoint size.
Pulse rapid, may be irregular.
Respirations very slow, may be six to eight per minute.
Temperature normal or subnormal.
Urine normal.
No hemiplegia.

Differentiate epilepsy from hysteria.

Epilepsy: In epilepsy there is complete loss of consciousness; the convulsions are at first tonic and then clonic; the pupils are dilated during the attack; the patient often bites his tongue. The attack may be ushered in by an *aura.*

Hysteria: In hysteria the loss of consciousness is never complete—the patient is conscious of his or her surroundings; the convulsions are not characteristic; the pupils are irregular; areas of anesthesia can be detected. The patient, who is usually a woman between the ages of fifteen and twenty-five, never hurts herself in falling.

Define catalepsy and give its etiology.

A condition in which the limbs are plastic and remain in any position in which they are placed. It occurs in hysteria, hypnotism, epilepsy, some organic diseases of the brain, and certain forms of insanity.

Differentiate tonic and clonic spasms.

Continued contractions are termed *tonic;* intermittent, *clonic.*

What is the significance of the patellar reflex as a sign of disease?

The knee jerk is *increased* in organic disease of the pyramidal tracts; lesions of the cord above the lumbar enlargement; disseminated cerebrospinal sclerosis and lateral sclerosis; mania; hysteria; strychnine poisoning; and spinal meningitis. The reflex is *diminished* or *absent* in posterior sclerosis; poliomyelitis (the anterior horns are part of the reflex center); myelitis; poisoning from drugs which destroy the cord, as antimony and chloral; pernicious anemia; degeneration of the muscle, as pseudomuscular hypertrophy and neuritis.

Outline the rehabilitation program of the hemiplegic.

(1) Footboard, or posterior leg splint, to prevent foot-drop; (2) sandbags to prevent outward rotation; (3) a pillow in the axilla to prevent adduction of the shoulder; (4) pulley therapy, which has an advantage over the usual stretching and passive exercises, in that the range of motion can be increased and adhesions prevented; (5) ambulation, which includes practice in balancing in the standing position, walking with the aid of parallel bars, learning a heel-and-toe gait to minimize clonus and re-establish normal walking habits, and using a short leg brace to help correct foot-drop; (6)

crutch walking; and (7) elevation, stressing climbing steps, curbs, stairs, and ramps. (8) Speech therapy, if indicated, should be instituted.

Discuss the treatment of epilepsy.

The treatment of epilepsy consists of the removal of causative and precipitating factors, regulation of physical and mental hygiene, and the use of anticonvulsant drugs.

Removal of Causative and Precipitating Factors: Infections of the central nervous system (syphilis, meningitis) should receive appropriate antimicrobial therapy. Disturbances elsewhere in the body, such as adenomas of the pancreas, hypothyroidism, hypoparathyroidism, etc., should be corrected. Lesions in the brain (tumor, abscess, vascular lesions, cortical scars, lesions secondary to trauma, etc.) should be removed surgically. Emotional factors, such as fear, feelings of incompetency, unfulfilled ambitions, domestic worries, etc., should be eliminated.

Regulation of Physical and Mental Hygiene: The prevention of physical and mental stagnation requires such measures as regular eating and sleeping habits, physical exercise and regular work (children should, if possible, continue in school). Alcohol beverages are forbidden. The epileptic should not drive an automobile or operate unguarded machinery, but, with proper safeguards, may participate in practically all kinds of sports, including horseback riding and swimming. Simple psychotherapy helps to overcome the feelings of inferiority and self-consciousness. The patient should know that many epileptics are leading normal, useful lives.

Anticonvulsant Drugs: Approximately 75 per cent of patients with convulsive seizures can have their attacks controlled or reduced in frequency with the proper use of anticonvulsant drugs. Certain of these drugs are more effective in one type of seizure than they are in another. In some instances, a combination of drugs will prove more effective than the use of one alone, the dosage varying with individual patients. When changing from one drug or a combination of drugs, the dosage should be gradually increased and, at the same time, the old drug or drugs gradually decreased, as a sudden withdrawal may precipitate an attack of status epilepticus. For those patients with infrequent grand mal seizures, phenobarbital (0.1 to 0.2 gm. daily) is best tried at first, but if the seizures become more frequent, diphenylhydantoin sodium (Dilantin sodium) (0.1 gm. 3 times daily, or more, but not to exceed 0.6 gm. daily) should be given in combination or alone. At times, methylphenylethylhydantoin (Mesantoin), alone or in combination with diphenylhydantoin, will prove more effective. The same dosage is used for both drugs, although larger amounts of methylphenylethylhydantoin may be tolerated. For petit mal seizures, the drug of choice is trimethadione (Tridione) or its homologue (Paradione), 0.6 to 3.0 gm. daily for either drug. When patients are subject to both grand mal and petit mal seizures, they should receive trimethadione or Paradione plus diphenylhydantoin sodium, methylphenylethylhydantoin, or phenobarbital.

Describe aphasia.

Inability to utter words or to comprehend them.

Sensory Aphasia: Word blindness, inability to recognize written or printed words; *word deafness,* inability to interpret spoken words.

Motor Aphasia: Inability to utter words, although knowing their meaning.

Paraphasia: The misuse of words or syllables.

Aphasia occurs in any injury to the brain; hemorrhage, thrombosis, embolism, abscess, tumor involving the center of speech, or Broca's region, and in hysteria.

Outline the treatment of parkinsonism (postencephalitic, idiopathic, and arteriosclerotic).

Parkinsonism, regardless of cause, is a noncurable and difficult-to-treat disease, in that such factors as the age of the patient, multiplicity of symptoms, and the tendency for the drugs to build up tolerance in a patient make therapy more a problem of management than of specific treatment.

(*1*) *Drugs:* At this time, the synthetic parasympatholytics, owing to somewhat lower toxic effects, are the best form of therapy for this group. Trihexyphenidyl (Artane), cycrimine hydrochloride (Pagitane), and caramiphen hydrochloride (Panparnit) are used in succession, holding each level of dosage until it loses its effect and then increasing it, as tolerated. The total dosage varies with the individual. A second preparation is then slowly substituted and, as it loses its effect, a third, etc. In addition, other drugs are employed as adjuncts to these antispasmodics to relieve agitation and insomnia, such as the antihistamines (diphenhydramine hydrochloride [Benadryl]), anti-anxiety agents (meprobamate [Miltown]), or a curare-like drug, mephenesin (Tolserol), for severe rigidity.

(*2*) *Psychotherapy:* In this disease this is important. The patient should have as thorough an understanding as possible of the nature of his illness and the importance of his cooperation in drug therapy.

(*3*) *Surgery:* The inadequate results of medical therapy have led to the introduction of various operative procedures. As yet these procedures have not been standardized and there is no fixed criterion for selection of cases. The best results have been obtained in patients whose symptoms are completely, or almost completely, confined to one side of the body and who are under the age of 60 years.

Define and list the common causes of syncope.

A symptom complex characterized by a sudden transitory weakness, faintness, dizziness, and lightheadedness, culminating in falling and unconsciousness unless the process is interrupted before this stage is reached. Syncope may result from: (1) fall in arterial blood pressure—orthostatic hypotension, hemorrhage, severe pain, injury, response to fright, etc.; (2) cardiac disturbances—paroxysmal tachycardias, Adams-Stokes syndrome, aortic insufficiency and stenosis, etc.; (3) cerebral circulatory or metabolic disturbances—carotid sinus reflex hypersensitivity, migraine, hypertension, anoxemia, anemia, hypoglycemia, methemoglobinemia, etc.; (4) hysterical or anxiety states—fainting often follows hyperventilation, which is usually either a hysterical conversion symptom or a concomitant of anxiety.

Give a short outline of the symptomatology of dementia paralytica.

The symptomatology varies greatly. Onset may be insidious or abrupt. So-called "typical cases" are described in three stages, which, however, are quite arbitrary.

(*1*) *State of Onset:* Change in the personality occurring in an adult, change in manner, irritability, lack of neatness and cleanliness, inability to concentrate, slowness of comprehension, lack of judgment. Neurasthenic symptoms. Depression or elation.

Headache, disturbance of vision, tremor of hands, and slight loss of coordination resulting in faulty enunciation. Change in facial expression. Pupillary changes are variable. Argyll Robertson pupil is only rarely present. Tendon and skin reflexes also vary.

(*2*) *Stage of Full Development:* Euphoria; delusions of grandeur or, on the other hand, depression; fear of impending disaster; and self-accusation. Simple dementia. Paranoia. Epileptiform or apoplectiform, so-called *paretic seizures,* with temporary paralysis. Disturbances of reflexes more marked—ankle clonus hyperactive, knee jerks, Babinski's sign.

(*3*) *Terminal Stage:* Progressive weakness, emaciation, bed sores, general paralysis of all the muscles. Death results from intercurrent disease, paretic seizure, or paralysis of the respiratory muscles.

Give the symptoms and treatment of tabes dorsalis.

Symptoms: Loss of coordination; inability to stand with the eyes closed and feet close together (*Romberg's sign*); the arms may be affected; the patient is unable to touch the tip of his nose with his eyes closed; characteristic gait; no loss of power; sharp, *lancinating pains* appearing in paroxysms, especially around the body—so-called *girdle pains;* pain in the abdomen with vomiting—so-called *gastric crises*—also occurs. Paresthesia is observed in various parts of the body. The *knee jerk* is lost, and the *Argyll Robertson pupil* is present. There may be diplopia, dimness of vision from optic atrophy, and paresis of the ocular muscles. As the disease progresses, sexual power is lost; the patient develops epileptiform seizures and ultimately dementia.

Treatment: Penicillin, in any of its forms, is the treatment of choice: procaine penicillin G, 600,000 units intramuscularly daily for 14 to 21 days, or benzathine penicillin G 1,200,000 units intramuscularly twice weekly for 3 weeks. The response to treatment varies with the extent of the syphilitic involvement. In "burned out" tabes dorsalis, in which a normal cell count and protein level in the spinal fluid indicate that the inflammatory process has completely subsided, one would expect little effect upon the residual manifestations from any form of therapy. However, improvement in some symptoms, such as pain, may occur following penicillin treatment.

What are the causes, symptoms, and prognosis of Bell's palsy?

Causes: (1) Lesion of the facial center in the cortex or the nucleus of the facial nerve—tumor, clot, or abscess. (2) Paralysis of the facial nerve in the petrous portion of the temporal bone from fracture or extension of inflammation of the middle ear. (3) Inflammation of the peripheral filaments of the nerve from exposure to cold, injury, rheumatism, or one of the infectious fevers.

Symptoms: The condition is readily recognized. The affected side is smooth and expressionless; the angle of the mouth droops; the eye cannot be closed; tears flow over the cheek; and the speech is affected on account of the inability to control the lips. When the lesion is central, the upper part of the face escapes and other cranial nerves are involved. When the lesion is in the fallopian canal, there may be loss of taste in the anterior part of the tongue and deafness or hyperacousia. When the peripheral filaments are affected, the paresis is complete and reactions of degeneration are present.

Prognosis: This depends on the cause; it is regarded as favorable when the palsy is due to peripheral neuritis. If the palsy is central, the prognosis is grave, except in cases amenable to treatment, such as syphilis. Recent reports suggest that cortisone accelerates recovery in some patients.

Give the treatment of trigeminal neuralgia (tic douloureux).

Palliation: In the early stages, palliative measures are employed but are usually unsatisfactory and surgical intervention is necessary. Temporary relief sometimes follows the inhalation of trichloroethylene, 20 drops on gauze until the odor disappears, before meals; vitamin B_{12}, 1,000 micrograms intramuscularly daily; nicotinic acid in flushing doses before meals; ferrous carbonate orally (4 gm. twice daily); stilbamidine intravenously (150 mg. in 500 cc. of saline solution daily for 7 to 14 days); or pyridoxine hydrochloride orally (50 mg. 3 times daily). In addition, mild sedation with phenobarbital, but narcotics should only be used as an emergency measure, for addiction is a real danger.

Surgical procedures:

(1) Alcohol injection of the nerves near their exits from the skull (said to give relief for 9 months).

(2) Alcohol injection of the gasserian ganglion (relief usually permanent).

(3) Peripheral avulsion of the sensory root (relief for 9 months).

(4) Radical division of the sensory root (permanent relief).

What is Horner's syndrome?

Retraction of the eye into the orbit (enophthalmos), contraction of the pupil (miosis), sympathetic ptosis, and absence of sweating caused by a lesion of the ciliospinal center, which is situated in the eighth cervical and first thoracic segments.

Horner's syndrome is caused by paralysis of the center. During the preceding irritative stage the signs are reversed: exophthalmos, mydriasis, and a wider palpebral fissure than in a normal eye.

Any lesion, whether from disease or trauma, that interferes with the reflex arc of the cervical sympathetic system will produce this syndrome. Syphilis is one of the causes. Horner's syndrome may be an early sign of tabes dorsalis.

Give the common causes of vertigo.

(1) Vertigo of labyrinthine origin (aural vertigo), Ménière's syndrome, drug intoxication (streptomycin, quinine, salicylates, etc.); (2) ocular disturbances, such as ophthalmoplegia with diplopia; (3) lesions in the cerebral cortex—aura of an epileptic seizure, brain tumor, etc.; (4) vertigo of brain-stem origin—multiple sclerosis, neoplasms, etc.

What is the most common cause of choked disk?

Brain tumor accounts for 90 per cent and the remaining cases are due to syphilis, meningitis, ependymitis, sinusitis, anemia, etc.

Differentiate between Ménière's syndrome and brain tumor.

The cardinal symptoms of Ménière's syndrome are paroxysmal attacks of vertigo, associated with tinnitus and deafness. The dizziness and vertigo associated with brain tumors (acoustic nerve, cerebellum, or brain stem) are not paroxysmal in nature. In addition, these lesions are accompanied by signs and symptoms of injury to other structures in the nervous system.

Describe the gait associated with cerebellar disease.

A reeling or drunken gait; if the cerebellar involvement is unilateral, the patient has a tendency to veer toward the side of the lesion.

What is the significance of the absence of abdominal reflexes?

The loss of the abdominal reflexes is common in acute abdominal conditions and often in the obese and in those whose abdominal walls are relaxed and atonic (pregnancy). Otherwise, loss of abdominal reflex means an interruption in the reflex arc—anterior horn disease or involvement of the pyramidal tract. In the presence of other signs, the absence of abdominal reflex in a young person suggests multiple sclerosis.

Discuss the diagnosis of amyotrophic lateral sclerosis.

This disease usually occurs in middle life and is characterized by weakness of the hands and arms, difficulty in talking and swallowing, weakness or spasticity of the legs, or a combination of all or some of these symptoms. Examination in a typical case reveals diffuse muscle atrophy varying in intensity in various parts, diffuse fasciculations, pyramidal-tract signs varying from well-marked leg spasticity to merely overactive reflexes and Babinski signs, bulbar signs, and absence of sensory disturbances. Certain diseases may be readily confused with this condition. Syphilitic amyotrophy may produce a similar picture but is usually symmetrical, is often associated with Argyll Robertson pupils, and the spinal fluid will show evidence of syphilis. Myasthenia gravis is differentiated by a history of easy fatigue of the involved muscles, absence of atrophy and fasciculations, and by an effective response to a test dose of neostigmine methylsulfate (Prostigmin). Cervical cord tumor is differentiated by root pains in the arms, absence of diffuse fasciculations, presence of sensory disturbances and the demonstration of subarachnoid block. Herniated cervical disk may be differentiated by the presence of pain in the arm, unilateral motor and reflex signs, and narrowed intervertebral disks.

Describe the symptoms and treatment of hydrocephalus in children.

Symptoms: The disease may be present at birth, and the large head interfere with delivery. The head is globular; the fontanels and sutures remain open, and the face is relatively small; the eyes protrude and are rotated downward. The weight of the head interferes with the child's movements. The intellect is impaired; exceptionally there may be precociousness. The reflexes are exaggerated; spastic paralysis may be present, and convulsions sometimes develop.

Treatment: Medical treatment is unsatisfactory and, although surgical attack is hazardous, recoveries have been observed after opening the wall of the third ventricle.

What does the term combined system disease designate?

Combined system disease (subacute combined degeneration of the spinal cord, funicular degeneration of the spinal cord, subacute combined sclerosis) is primarily a degeneration of the dorsal and lateral columns of the spinal cord, resulting in an ataxia of the lower limbs with variable degrees of spasticity and weakness, progressing to severe paraplegia in flexion, if unchecked. The disease is due to a deficiency in the absorption and utilization of vitamin B_{12} and is seen most often with pernicious anemia in patients in, or after, middle life. In addition, the characteristic symptoms may occur in pernicious tapeworm anemia, sprue, pellagra, and diabetes mellitus.

Discuss symptomatology and diagnosis of multiple sclerosis.

The *symptoms* may resemble either those of locomotor ataxia or those of lateral sclerosis, depending on the part of the cord chiefly affected. The characteristic symptoms are spastic paraplegia with exaggerated reflexes, vague pains, a coarse tremor developing on movement, slow wasting, "scanning" speech, nystagmus, sometimes diplopia, and sometimes paralysis of the ocular muscles, mental impairment, and loss of sphincter control, notably of the bladder. Since there are no laboratory tests specific for multiple sclerosis, the diagnosis rests on the history and physical findings, not always an easy matter, considering that the condition has earned a reputation of being "a disease scattered in time and space." In general, the diagnosis depends on the finding of separate discrete lesions in various parts of the nervous system, with additional separate focal lesions developing over a period of time.

Give symptoms and management of acute chorea (St. Vitus' dance, Sydenham's chorea).

Usually, the symptoms develop slowly and insidiously; fragmentary movements of the lips, tongue, cheeks, and eyes, twists and nods of the head, and unexpected finger movements are common early manifestations of the disease. Later, the degree and frequency of these so-called "choreic" movements become more pronounced and spread to other parts of the body with interference in walking, speaking, swallowing, or any part of the motor apparatus. In general, the movements are spontaneous, abrupt, purposeless, and irregular and occur both at rest and with voluntary activity, but cease during sleep. Mental symptoms include irritability, restlessness, emotional instability, carelessness, poor memory (sometimes dullness and inattention), hysterical outbreaks, and, in severe cases, a picture that resembles a delirium or a hypomanic reaction. Most cases run a course of 6 to 8 weeks with recurrences noted in about one third. Certain symptoms may linger on and are accentuated in periods of undue stress and strain. This is particularly true of patients with personality changes. Since there is no specific therapy of chorea and it is a self-limited disease, treatment consists for the most part of rest. In the less severe cases, this can be accomplished at home under proper supervision, the degree of activity being dependent on the presence of an associated acute rheumatic fever. The more severe cases should be hospitalized with complete bed rest, isolation, and mild sedation. In addition, hot packs, warm baths, electric blankets, and continuous flow baths are often helpful. Fever therapy in the form of intravenous typhoid vaccine seems to shorten the course of the severe cases. Recently, ACTH, cortisone, and their related compounds have been recommended for the refractory case, although the benefits are as yet debatable.

Discuss the classification of mental disorders.

The following is suggested as a brief and practical classification based on etiology:

A. *Organic Psychoses:* Comprising those types in which there is evidence of actual brain injury, as paresis, senile dementia, syphilis.

B. *Toxic Psychoses:* Resulting from alcohol and other drugs; the toxins of acute infections (delirium); industrial poisons; toxins due to metabolic or endocrine disorders.

C. *Psychogenic Psychoses:* Those in which no organic or toxic factors are demonstrable, as schizophrenia and manic-depressive psychoses, as well as many of the psychoneuroses and psychosomatic cases.

Discuss the terms psychosis and psychoneurosis.

Psychosis: A severe, protracted, or even permanent mental disorder with complete disorganization of the personality, such as manic-depressive psychosis and schizophrenia (*dementia praecox*). Some psychoses are due to organic disease, while other types are solely psychogenic in origin.

Psychoneurosis (or, Simply, Neurosis): A relatively mild behavior disorder of purely psychogenic origin presenting the symptoms of a so-called "functional" neurological disturbance, such as hysteria, neurasthenia, or psychasthenia. The personality remains intact; the patient is only partially incapacitated, and, as a rule, does not need institutional treatment.

Mention some characteristics of mental or emotional pain (psychalgia) which would aid in its differentiation from bodily pain or somatalgia.

The pain is constant but varying in intensity, described by the patient as "peculiar" and rather a "tension" than a pain; tends to disappear with subsidence of the emotional cause. The distribution is uncertain, vague, and difficult to describe, sometimes entirely at variance with anatomical factors (glove or sleeve anesthesia in hysteria).

Give four examples of a psychoneurosis.

(1) Conversion hysteria. (2) Neurasthenia. (3) Compulsion neurosis. (4) Anxiety neurosis.

Define and differentiate illusion, delusion and hallucination.

Illusion: A false or misinterpreted sensory impression; a false interpretation of a real object.

Delusion: A false belief that cannot be corrected by argument, or persuasion, or even by the evidence of the patient's own senses. A settled belief in facts that have no existence and which no normal, rational person believes.

Hallucination: A false sense perception not founded on objective reality. The sensation may be auditory ("voices"), tactile, gustatory, olfactory. Stump hallucination, feeling a part of the body after its amputation; reflex hallucination (the patient on feeling a sensation of one kind experiences a second, entirely different sensation).

What are the character traits of individuals classified as pathologic personalities without actual mental disorders? Give some examples.

Increased emotional response to stimuli with lessened inhibition and voluntary control. The "super-ego" fails to control the "id." Impulsiveness, poor judgment, inability to realize the possible consequences of asocial acts, or, if realized, indifference to such consequences.

Examples: With pathological sexual drive—rapists, sexual perverts of various types, homosexuals, etc.

With pathological emotional response —bullies and braggarts, practical jokers, sadists, sly, cunning individuals.

With amoral rather than immoral, and with asocial, impulses—forgers, kleptomaniacs and pilferers, pyromaniacs.

What is combat fatigue?

A neurosis brought on by the stresses of military life or by wounds sustained in battle. It presents certain special features that must be borne in mind: The psychiatrist is dealing with "normal" men, since the personnel are rigorously screened before induction—normal, that is, in a civilian environment; the patients are all young or in early middle life; the breakdown may, and frequently does, come on *after* separation from the service or during a furlough, after the man has returned home temporarily or permanently; the prognosis is better than in most other neuroses. Combat fatigue responds well to psychoanalytic treatment.

External Causes: Exposure to danger, injury, and disease; separation from home and friends; the unavoidable regimentation and petty restrictions of military life; actual battle injuries.

Internal Causes: Homesickness, boredom, unsatisfactory relations with superiors, and, especially, frustration and resentment or even rage. Separation from wife and children in the case of married men constitutes a special hazard, which is a frequent cause. The effect is a general weakening of emotional control in individuals who have failed to achieve "maturity."

As in all neuroses, the type of reactions and symptoms is determined by the individual personality traits present since childhood and further developed by family relationships, education, and early experiences. "Every man has his specific emotional vulnerability." One who adapts well to civilian life breaks down when exposed to the stresses and strains of military discipline and to the dangers and horrors of the battlefield, while others find the orderly routine of army life, in spite of its drawbacks, or the thrill and excitement of combat a welcome relief from their former life and make good soldiers.

Outline the causes and treatment of insomnia.

The causes of insomnia may be defined as *somatic,* in which sleep is interfered with by physical causes, either outside the person (noises, bright lights, excessive heat or cold, etc.), or inside the person (undue fatigue, pain, hunger, fever, etc.); and *psychological* factors, which include both conscious causes (excitement, anxiety, anger, guilt, fear, unsatisfied desire, etc.) and unconscious causes (neurotic and psychotic insomnia). Treatment of insomnia is divided into efforts to remove the causes and methods of counteracting them. Sedatives are advocated in certain instances, such as in the conscious psychological group, whereas psychotherapy is employed in neurotic insomnia. Patients with psychotic insomnia are best handled by psychiatrists.

Outline the management of psychoneurosis.

(1) Detailed history and complete physical examination, in order to be able to assure the patient that no organic disease is present; or, if some organic con-

dition is present, the patient can be told just how much it is responsible for his symptoms. In addition, the source of the patient's anxiety and tension may be uncovered, although this usually requires subsequent interviews, at which time the patient is encouraged to unburden himself and ventilate his conflicts.

(2) Drugs are employed to relieve the patient's tension and anxiety (phenobarbital or meprobamate [Miltown]) and to reduce any dysfunction that may be present in a certain organ as a result of tension (belladonna).

(3) Environmental manipulation and re-education. Very often the emotionally upset patient will present a distorted picture of his environment, whether home or occupation. In such instances every effort is made to ascertain the true picture and make recommendations accordingly. Furthermore, the physician should evaluate the patient's assets and liabilities and lead him into some suitable constructive work or hobby that will divert his energies from preoccupation with himself.

What is understood by the term "the epilepsies"? Give the treatment of the epileptic psychoses.

Epileptiform convulsions occur in many pathological conditions other than idiopathic or genuine epilepsy. Such seizures are called by psychiatrists "the epilepsies" and occur in such conditions as general paresis, cerebral syphilis and brain tumor, uremia, eclampsia, etc.

Diagnosis is important. The differential diagnosis between true epilepsy and hysteria is given on page 303. Among the newer special methods the study of brain waves by electroencephalography and the Rorschach test should be mentioned.

Epileptic Psychoses: These manifest themselves in various forms ranging in severity from mere periodic disturbances of the personality to severe anxiety and maniacal states; epileptic dream or twilight states; delirious confusion with hallucinations; mental deterioration and actual dementia, which may take the place of the classic grand mal seizures and are spoken of as *"epileptic equivalents."* In the so-called "conscious delirium" or "fugue state," fortunately rare, the patient may commit criminal acts, of which he later has no recollection and for which he may become involved with the law. In the worst cases of this kind, *"epileptic furor,"* the patient becomes maniacal, destructive, and even homicidal, sometimes committing the most atrocious crimes. Paranoid states are also common.

Treatment of Psychotic Epileptics: Preventive treatment before the development of convulsive seizures, in the so-called "epileptoid" state, offers some prospect of success. Such individuals may be recognized by their epileptic personality traits: egotism, self-conceit, emotional instability, hypochondriasis. The family history may furnish a hint; the theory of heredity still has some adherents. For principles of specific treatment, see treatment of epilepsy, page 304.

Mention and define a psychosis with a definite alcoholic etiology.

Korsakoff's Psychosis: Occurs in chronic alcoholics. Characterized by abnormal suggestibility and susceptibility to external stimuli, faulty memory, hallucinations. It is also called "chronic alcoholic delirium" and "polyneuritic psychosis." Wrist-drop and other signs of polyneuritis are often present.

What is involutional melancholia?

A psychosis of middle life occurring especially in women during the climacteric. It comes on earlier in women (40 to 55) than in men (50 to 65). It is characterized by anxieties, depression, sometimes profound (suicidal attempts occur), self-accusation, depondency, somatic and nihilistic delusions, and delusions of persecution. Catatonic symptoms, negativism, stereotypy, and catalepsy are sometimes present. Insight is poor.

Give a brief description of paranoia.

"A fixed type of disease due exclusively to internal causes and characterized by persistent systematized delusions, the preservation of clear and orderly thinking and acting and by absence of hallucinations." (Kraepelin.)

Paranoia is a rare disease of middle life, more common in men, chronic and incurable, with violent and often homicidal tendencies. Homosexuality is said to be a frequent underlying cause. The delusions (of persecution, grandeur) of paranoia are systematized. Orientation as to time, space, and person is preserved; memory and the faculty of thinking and reasoning are not disturbed. Paranoiacs are abnormally suspicious, given to imputing sinister motives to ordinary, innocent words and acts on the part of others, fond of litigation (danger of financial losses), and potentially dangerous. The disorder is slowly progressive and may take years to manifest itself (danger to environment and community).

Treatment: Hospitalization is essential both for the protection of the patient and that of the community. On account of possible legal complications commitment by court order is often advisable. Psychiatric treatment is not promising; psychoanalysis, explanation of previous experiences, and persuasion may be of help in the early stages.

Discuss the psychotic features of general paresis and methods of treatment.

The type of psychosis, especially in the early stage, will be determined by the personality pattern in the individual case: the extrovert of sanguine temperament tends to develop a psychosis of the manic type, with delusions of grandeur and extravagant ideas and actions; the seclusive, pessimistic type is more likely to end up having a case of melancholia with paranoid tendencies. The initial symptoms in nearly all paretics are irritability, impaired memory, faulty judgment, and general mental and moral deterioration. As the disease progresses, delusions of various kinds—of grandeur, persecution, paranoid, etc., develop, and in most cases unfortunately, total dementia closes the scene.

Treatment: Since the principal cause of neurosyphilis is the neglect of antisyphilitic treatment in the early stage of syphilis, 15 to 20 years before the onset of mental symptoms, the prognosis is of course not good; nevertheless arrest of the disease and even clinical cures are sometimes obtained by the intensive use of modern methods of treatment. Of these *penicillin* offers the best results either alone or in combination with artificially induced *fever*. At present the trend is away from the use of heavy metals with penicillin.

Describe and give treatment of schizophrenia.

A psychosis of early adult life (*dementia praecox*), of psychogenic origin, characterized by a "split personality," various behavior disorders, withdrawal from reality (seclusiveness) and, in its later stages, delusions and hallucinations. Heredity as a cause is debatable. The prognosis, while in general unfavorable, is not hopeless, and recovery with return to a normal life is possible after appropriate treatment.

Schizophrenia occurs in subjects with a psychopathic, "schizoid" (introvert) personality, the first manifestations of which may be noted in early childhood. Such children are shy, noncooperative with other children, especially at play, "queer." Mental powers may not be affected and some individuals may even be exceptionally well-endowed intellectually and artistically. It is one of the most common psychoses. It usually begins in early adult life and at first may not interfere with ordinary normal living and useful activities. As the disease progresses, however, the patient becomes more and more seclusive; the typical picture of schizophrenia develops, with disorders of speech, behavior, and thinking—phantasies (day dreaming), negativism, mutism, preoccupation and perseveration, projection, symbolization, ideas of reference. Later the typical delusions of persecution and grandeur and hallucinations supervene; the course of the disease is steadily deteriorating and ends in complete dementia. Violence and suicidal and homicidal tendencies are less common in schizophrenia than in some other psychoses.

Four types are described: (1) *Simple:* apathy, lack of interest in surroundings and noncooperation; no delusions or hallucinations. (2) *Hebephrenic:* the early type, beginning in childhood. (3) *Catatonic:* negativism, stereotypy, attacks of excitement alternating with stupor, catalepsy; delusions and hallucinations. (4) *Paranoid:* beginning much later; systematized delusions of persecution and grandeur prominent; hallucinations.

Treatment: Hospitalization is necessary in most instances to obtain therapeutic results, although selected cases of schizophrenia may be managed in the office, especially since the advent of the tranquilizing drugs. However, commitment by court action may become advisable to protect the patient's interests (unwise investments, extravagance, litigiousness, etc.). For the most part, treatment consists of drugs, alone or in combination with electroconvulsive therapy, psychotherapy, and general medical care (since schizophrenics have a great tolerance to the tranquilizing drugs, it is necessary to give relatively large doses). Chlorpromazine (Thorazine) and reserpine (Serpasil) are the drugs of choice and can be given orally or intramuscularly. Since their effects are so similar, the drugs can be exchanged one for another and it is possible to combine the two, which has proved beneficial in certain instances. Both drugs are frequently associated with parasympathetic phenomena—nasal congestion, increased salivation, abdominal cramps, diarrhea or constipation, dizziness, drowsiness, generalized tremulousness, edema of face and feet, sensation of pins and needles in the extremities, convulsive seizures, and symptoms of parkinsonism. Jaundice and agranulocytosis may follow chlorpromazine. Most of the symptoms are mild and often disappear during therapy. In the presence of jaundice, agranulocytosis, or signs of parkinsonism, treatment must be discontinued. With both drugs, it seems advisable to start with relatively small doses: chlorpromazine 25 mg. by mouth, three times daily, increasing the dosage gradually every 4 to 6 days, as indicated. A total daily dosage of 800 to 1,000 mg. may be given. The intramuscular route is often employed in selected cases during the first 24 hours of treatment (2 cc. = 50 mg.) for 2 to 3 doses. Reserpine may be given 0.25 mg. by mouth four times daily for the first 7 to 10 days and then increase as needed, up to a total dose of 8 mg. daily. In severe cases, intramuscular injection of reserpine (2 cc. = 5 mg.) may be necessary.

Give a brief general description of manic-depressive psychosis, including etiology and treatment.

Synonyms: Mania and melancholia; circular insanity; affective psychosis; alternating or circular psychosis.

A rather common, relatively mild psychosis with a tendency to recovery and recurrence. Occurs mainly in individuals of "extrovert" ("cycloid") personality: sanguine, energetic, sociable, healthy, and robust of the so-called "pyknic" body-type. The patients alternate between periods of exaltation, excessive talkativeness, and motor activity and periods of deep dejection and melancholia. Delusions and hallucinations, violence, and homicidal and suicidal tendencies are uncommon except in very severe cases. The main symptoms are emotional instability, frequent and sudden changes of mood, irritability, and, in the depressive phase, deep dejection, hopelessness, self-accusation, and a sense of guilt. The disorder is more common in women.

Etiology: The most commonly accepted theory is an inherited and familial predisposition, as described. Other authorities assume an essentially psychogenic cause, a conflict between "id" and "super-ego": in the depressive phase punishment by the ego for past transgressions; in the manic, rebellion of the unconscious against the domination of the super-ego.

Depressive Phase: At first, retardation of speech and motor activity going on to dejection rather than depression, feeling of inferiority, tendency to self-accusation, hopelessness, hypochondriasis. Insomnia, anorexia and loss of weight, and constipation in some cases. Later, neglect of personal appearance; increased slowing of mental processes and of speech; libido also lessened. Delusions of an incurable disease and hallucinations—auditory, olfactory or somatic—may occur. Suicidal ideas; it is usually in this phase that suicide occurs, if at all. The depression may be interrupted by periods of great restlessness, motor agitation, pacing up and down, wringing of hands, self-mutilation. In a final stage—depressive stupor—these features are exaggerated: the patient becomes completely apathetic, refuses to eat or talk and forced feeding becomes necessary.

Manic Reactions: Hypomania, acute mania, and hypermania or delirious mania are described.

HYPOMANIA: There is increased speech and motor activity, aggressiveness, boasting, irritation and resentment when crossed. In this stage treatment at home or on a farm or ranch may still be possible.

ACUTE MANIA: In this stage overactivity, combativeness and destructiveness, and alcoholic and sexual excesses are added to the usual symptoms; "flight of ideas," profane and obscene language. Bodily complications, as mentioned above, anorexia, loss of weight, insomnia develop. Delusions and hallucinations uncommon. Memory, sensorium, insight, and general information relatively unaffected.

HYPERMANIA: The symptoms are greatly exaggerated. The patient becomes incoherent and excessively distractable, jumps from one idea to another, unable to complete a speech or act before another suggests itself. The manic attacks increase in frequency with the years.

Treatment: The outlook is said to be better when manic periods predominate. The better the basic personality and the earlier the onset of the disorder, the better the prognosis.

Shock treatment, preferably by *electroshock,* both in manic phase and in severe depressive conditions, is becoming the method of choice. Recovery or improvement may be expected about four weeks after the treatments are begun. Metrazol is also used but is being replaced by electroshock. Curare is necessary to guard against fractures.

After the convulsive treatment, psychotherapy is instituted. Owing to the patient's mental confusion, usually present during the period of shock treatment, psychoanalytic methods are unsatisfactory during the intervals between electroshocks.

General Medical Care and Supervision: Endocrine medication when indicated by somatic signs and symptoms, and above all nutrition (loss of weight, dehydration) must of course never be neglected. Forced feeding is often necessary. Sedation for insomnia and limiting the activities is best achieved with chloral hydrate or paraldehyde. The tranquilizers—reserpine (Serpasil), chlorpromazine (Thorazine), meprobamate (Miltown), etc.—have proved useful in excited patients, in that they produce tranquility without sedation.

Definitions

It is to be borne in mind by the student that modern psychiatry is still in the stage of development and that nomenclature, as well as classification, is not finally fixed nor generally accepted. There is a tendency for every worker in the field to have his own special definition for a given concept and his own special interpretation. It is therefore often necessary to give more than one definition.

For convenience the alphabetical arrangement has been adopted.

AFFECT: The feeling experienced in connection with an emotion. The degree or quantity of feeling; the measure of emotional capacity or reaction to a given situation or event. Also called "feeling-tones."

ANARTHRIA: Loss of ability to speak, in contrast to aphasia, which is the inability to speak or write words which were once familiar.

AUTISTIC THINKING: Dream or phantasy thinking; daydreaming, as contrasted with realistic thinking.

BRADYPHRENIA: Slowing up of mental processes or "mentation."

CATALEPSY (*flexibilitas cerea,* "waxy" pliability or rigidity): A condition characterized by a waxy rigidity of the muscles so that the patient tends to remain in any position in which he is placed.

CATAPHRENIA: Mental debility of the dementia type, which tends to eventuate in recovery.

CATATONY: A form of schizophrenia characterized by negativistic reactions, phases of stupor or excitement, and impulsive or stereotype behavior. See also *Catalepsy.*

CATHEXIS: Concentration of mental or emotional energy upon an idea or object. Mental tension.

COMMAND OR AUTOMATIC OBEDIENCE: Abnormal suggestibility, as in echolalia and echopraxia.

CHARACTER NEUROSIS: Character traits equivalent to formal symptoms, such as anxiety states, compulsions, obsessions, conversion hysteria.

COMPLEX: A system of ideas held together by strong emotional tone which, because not acceptable to the ego (conscious mind), has fallen into the unconscious.

A series of emotionally accentuated ideas in a repressed state (Freud).

COMPULSION: A recurring impulse to perform some act contrary to one's desire and judgment.

CONDENSATION: Fusion of events, thoughts, or concepts to produce a new and simpler concept.

CONVERSION HYSTERIA: Conversion of an emotional conflict into hysterical symptoms and signs by a process of repression and substitution.

CYCLOID: According to Kretschmer, those people who are subject to cyclic variations of mood; they are predisposed to manic-depressive psychosis.

DEPRESSIVE PSYCHOSIS: Psychosis characterized by melancholia and feelings of inadequacy, despondency, and guilt.

DREAMS: According to Freud (1) a psychic phenomenon, a form of communication from the unconscious; (2) the fulfilment of a suppressed wish.

ECHOLALIA: Repeating the exact words used by another person.

ECHOPRAXIA: Copying movements made by another person.

EGO: That part of the psyche which possesses consciousness, maintains its identity, and recognizes reality.

FAMILIARITY: The feeling of having been in a strange place before, or of having experienced an apparently new situation before.

FLIGHT OF IDEAS: A rapid change of ideas connected only by a superficial similarity in the sound of words or by environmental changes.

FUGUE: An abnormal mental state in which various logical acts, such as shopping, going on trips, etc., are performed apparently consciously, but of which the patient afterwards has no (conscious) recollection.

GRAPHOLOGY: The study of personality traits revealed in handwriting.

HYPERAKOUSIS: Extreme or painful sensitiveness to noise.

Id (Freud): The instincts (erotic and thanatotic); instinct of self-preservation; the true unconscious dominated by the pleasure principle.

Ideas of reference: The interpretation of ordinary, insignificant incidents or actions as having reference to one's self. Excessive suspiciousness. (cf. *Delusions of persecution.*)

Identification: A mechanism of the unconscious by which the ego transfers to itself qualities belonging to others. Also, the ego transfers to one person the representation it holds of another person or of itself.

Idiophrenic psychosis: Organic, due to disease of the brain.

Inferiority complex: A combination of emotionally charged inferiority feelings which operate in the unconscious to produce timidity and lack of self-confidence; or, as a compensation, exaggerated aggressiveness and expressions of superiority.

Insight: Ability to realize the nature and seriousness of one's illness.

Introjection: The appropriation to one's self of an occurrence or of a characteristic. Turning against one's self the hostility felt for another.

Libido: (1) Originally, the sexual desire. (2) The energy derived from the primitive impulses. (3) Psychic energy in general.

Mentation: Term suggested by Meyer instead of "mind," "thinking," "consciousness."

Narcissism: (1) Self-adulation to the exclusion or incompleteness of heterosexual love, sometimes called "ego-libido."

(2) Sexual excitement through admiration of one's own body.

Negativism: Resistance, noncooperation. Tendency to do the opposite of the obvious under the circumstances, or of what one is asked to do.

Neologism: Word made up by the patient and having meaning only for himself.

Nihilistic delusion: A false belief that a part of the body is missing.

Obsession: Preoccupation with an idea that morbidly dominates the mind, constantly suggesting irrational action, and that persists regardless of the patient's wish to get rid of it.

Organic psychosis: A psychosis due to a lesion of the central nervous system, such as general paresis.

Personality: That which distinguishes and characterizes a person: intelligence, mental energy, special interests, basic mood, social adaptability. The total reaction of a person to his environment.

Types: Syntonic (normal), alternating, double or dual, multiple, disordered, schizoid, cycloid, paranoid, hysteroid.

Hysteroid individuals exhibit *conversion hysteria,* sometimes "local hypochondriases" (several organs affected).

Perseveration: Constant repetition of an activity.

Preoccupation: Engrossment with the same topic, or group of topics, to the exclusion of ordinary environmental subjects, and to the detriment of useful activity. (See also *Obsession.*)

Projection: (1) A mental mechanism by which a repressed complex is disguised by being regarded as belonging to the external world or to another person.

(2) Objectifying the subjective, or imputing to others motives that are really one's own.

Psychasthenia: A so-called "functional" psychoneurosis characterized by feelings of fear, anxieties, obsessions, inadequacy, self-accusation—"depersonalization."

Psyche: The mind, including both conscious and unconscious processes.

Psychiatry: (1) That branch of medicine which deals with recognition and treatment of mental disorders. It includes the study of the whole mental organization—emotions, impulses, reactions, experiences and ideas.

(2) The study of mental energy as it manifests itself first as instincts, later as feelings and emotions.

Psychoanalysis: Separation or resolution of the psyche into its constituent elements. In practice the psychiatrist investigates the patient's past experiences, explains their significance and persuades the patient to carry out the indicated psychiatric treatment.

Psychobiology: The scientific study of the personality functions; the interaction of body and mind in the formation and function of personality (Meyer).

Psychocatharsis or simply Catharsis: Treating a psychoneurosis by "purging" the mind of the repressed material that is the cause of the symptoms. Encouraging the patient to tell everything associated with a given train of thought.

Psycholepsy: A condition characterized by sudden changes of mood tending toward depression.

Psychoneurosis or Neurosis: Relatively minor disorder of the psychic constitution (personality), less incapacitating than psychosis. Personality remains practically intact.

Psychoparesis: Mental weakness.

Psychopathic personality: A constitutional tendency to mental disorder. A type of personality marked by lessened voluntary control and increased emotional response to stimuli.

Psychosis: See p. 309.

Psychosomatic: Pertaining to the mind-body relationship; having bodily symptoms of psychic (mental or emotional) origin.

Psychosomatic medicine: The medical specialty which deals with the diagnosis and treatment of neurological and mental disorders complicating or caused by organic disease.

Reference: Same as *Projection.*

Rorschach's test: A test of intelligence and personality. A series of ten inkblot designs, some black and some in colors, is shown the patient, and he is asked simply to tell what he sees. From his answers and reactions certain conclusions are drawn about personality traits.

Schizoid: An unsocial, introvert type of personality (Bleuler).

Selective fatigue: Fatigue brought on by physical or mental effort in which one is not interested, although able to engage in any desired activity which may even be more strenuous.

Somatic delusion: A false belief that the body or some organ is being interfered with or is not functioning properly.

Stereotypy: Persistent repetition of senseless words or actions. (See also *Echolalia, Echopraxia.*)

Sublimation: (1) The working off or release of energy produced by unattainable desires in some activity acceptable to the individual and his ethical code.

(2) Deviation of sexual motive powers from sexual aims or objects to new aims and objects other than sexual (Freud).

Super-ego: That part of the psyche which acts as a monitor over the ego.

Transference: (1) The shifting of an affect from one person to another, or from one idea to another; especially the transferring by the patient to the physician of emotional tones of either affection or hostility (positive or negative), based on unconscious identification.

(2) In psychoanalysis the reproduction of forgotten and repressed experiences of childhood.

Unconscious: The "Id," q.v.

(1) That part of mental activity which includes primitive or repressed wishes (Freud).

(2) The repository of the previous experiences in the life of an individual.

Unconscious phantasy: May be originally formed in the conscious and repressed into the unconscious, or originally formed in the unconscious; daydreaming. (See *Autistic thinking.*)

Undoing: Attempt of the unconscious to wipe out experiences painful to the ego.

Verbigeration: Stereotyped repetition of words or sentences.

Section 7

PUBLIC HEALTH AND PREVENTIVE MEDICINE

Outline the objectives of periodic health examinations.

(1) Health education, to prevent disease; (2) early detection, since some diseases cannot be prevented but can be controlled; and (3) reassurance, to explain the fundamental disturbances that may be corrected or modified.

What factors tend to intensify the problems of public health?

(1) Concentration of populations as a result of the industrial revolution, necessitating organized services for drinking water, protection of food supplies, disposal of domestic wastes, and industrial diseases.

(2) Rapid communication, which has broken down the isolation of communities thereby making difficult the control of certain diseases.

(3) Advances in knowledge pertaining to the diagnosis and prevention of diseases in general.

Of what value are vital statistics to public health?

(1) Depiction of the life history of a people, (2) comparison of one community to another, (3) objective evidence of effective public health measures.

List the important factors concerned with further reduction in infant mortality.

(1) Antepartum care of mothers, (2) pre- and postpartum maternal instruction, (3) adequate care for premature infants, (4) encouragement of breast feeding, (5) milk depots with pasteurized milk, (6) medical supervision for all infants, (7) improved economic conditions, such as better housing, sanitation, etc.

What are the practical applications of genetics?

(1) Diagnosis on the basis of genetic data; (2) treatment with appropriate means, if any, on basis of the genetic diagnosis; (3) prognosis: furnishing advice about prospective marriages and prospective families; (4) prevention: institution of preventive measures against certain diseases and abnormalities on the basis of specific genetic backgrounds; (5) solution of medical and medicolegal problems, as Rh compatibility and the determination of nonpaternity by various blood agglutinogens.

List the specific disorders associated with travel.

(1) Motion sickness; this condition is a primary and the most frequently encountered disorder of travel, as motion is the common denominator of all forms of travel. (2) Disorders due to changes in barometric pressure; these may occur if the barometric pressure changes are substantial, particularly in airplane transportation, but may occur in a train or automobile ascending to and descending from high mountainous areas: (a) baro-otitis media and barosinusitis; (b) hypoxia; (c) anoxia; and (d) hyperventilation. (3) Disorders due to vibration; each form of travel has its vibration characteristics. (4) Disorders due to noise; excessive noise may give rise to temporary deafness and headache. (5) Temperature, humidity, and ventilation; excessive heat, humidity, and inadequate ventilation give rise to well-known discomforts.

Discuss the role of safety belts in preventing automobile fatalities.

It has been shown that the three main causes of fatalities in automobile accidents are being thrown out of the open doors; being thrown against or through the windshield; being thrown against the steering column. Safety seat belts enable the passengers to decelerate with the car instead of through or against it while the crumbling metal parts absorb the impact. Experts have predicted that between 50 and 75 per cent of lives could be saved by the installation and conscientious use of seat safety belts.

What precautions should be taken before allowing a patient to travel by air?

(1) Determination of the patient's basic tendency to develop symptoms in flight, as regards fatigue, anxiety, motion sickness, and obstruction to the middle ear; (2) medical evaluation as to the existence of certain diseases that may affect fitness for travel by air.

What is the value of the Master two-step exercise test?

Electrocardiographic changes after the standard or "two-step" test serve as an index of coronary circulation or blood flow to the myocardium. A positive test must certainly be interpreted as evidence of inadequate coronary circulation and has been shown to represent a warning of future cardiac difficulties, including myocardial infarction. The test, however, has proved disappointing in the evaluation of cardiac reserve.

Cite 5 methods of overcoming nutritional deficiencies in diets which occur on a widespread basis.

(1) Enrichment of flour with elements of vitamin B complex, (2) enrichment of milk through irradiation or (3) addition of vitamin D, (4) addition of iodine to salt, (5) addition of fluorine to the public water supply.

Mention some of the diseases to which artisans are especially liable.

Lead, arsenic, copper, and other forms of poisoning; pulmonary and bronchial affections from the inhalation of coal dust and other kinds of dust (miners, glass-blowers, etc.); emphysema from constant, excessive distention of the lungs (cornet players, glass-blowers).

Discuss the etiology of pulmonary carcinoma.

The rapid increase in incidence of pulmonary carcinoma during the last 25 years appears only partially accounted for by better and newer methods of diagnosis. A mass of evidence, chiefly statistical, indicts cigarette smoking, although the specific carcinogenic factor is unknown. Other suggested etiological factors include carcinogenic agents from atmospheric pollution in cities, or tarring of roads, late effects of pneumonitis of viral origin, and exposure to chromates, arsenicals, and cobalt.

In the pursuit of what trades is there a predisposition to pulmonary diseases?

All those trades that have to be carried on in ill-ventilated and overcrowded rooms or in damp quarters (sweat-shops, etc.); those which are attended with the production of dust and of noxious gases.

Define the word "nuisance" in a broad hygienic sense.

Anything that actually injures, or is likely to injure health, and admits of a remedy either by the individual whose act or omission causes the nuisance or by the local authorities.

Name some of the nuisances dangerous to health.

Gases and dust of an offensive, irritating, or poisonous nature emanating from industrial establishments or refuse. Smoke from factories and railroads. Collections of stagnant water, garbage, manure exposed to the air; exposed excreta in dilapidated privies (fly-breeding); ditches and swamps, which favor mosquito-breeding; dilapidated buildings and dumps, which offer a refuge for rats.

What is pneumonoconiosis and what measures can be employed for its prevention?

A chronic interstitial fibrosis of the lungs caused by the inhalation of different varieties of dust, especially the hard, sharp varieties, such as coal dust, stone, clay and iron dust. A number of popular terms are in use in the various industries: miners' asthma, miners' phthisis, etc. The condition predisposes to tuberculosis and may be coexistent with it. The symptoms are dyspnea and cough, becoming progressively worse; later, pain in the chest, greatly diminished expansion of the lungs, and complete incapacity to work.

Exhaust ventilation is the most important general preventive. For miners, quarrymen, ore handlers, and workers with drilling tools, various wet appliances, goggles, and respirators to prevent inhalation of the harmful particles are in use. Periodic physical examination of all workers employed in such industries are mandatory. If the worker is found to have developed anthracosis or silicosis, or even incipient tuberculosis, he must be immediately removed from any occupation in which there is exposure to dust.

Define the following: (a) silicosis, (b) anthracosis, (c) siderosis, (d) aluminosis, (e) byssinosis, (f) berylliosis.

(a) The condition produced by stone dust, quartz, etc.; (b) that produced by coal dust; (c) that produced by iron dust and filings; (d) that produced by clay dust; (e) that produced by cotton; (f) that produced by fumes and dusts of beryllium salts and alloys.

What is sewer gas? How does the inhalation of sewer gas in large quantities affect the system?

Sewer gas is a mixture of a number of gases—carbon monoxide, carbon dioxide, ammonium, and hydrogen sulfide—resulting from the decomposition of animal and vegetable matter. In itself, sewer gas does not cause disease, but, if it is present in the air in sufficient quantities, it acts injuriously by the deprivation of oxygen, causing anemia and other conditions due to deficient oxygenation.

Name 3 methods for the control of communicable diseases.

(1) Application of measures to interrupt the spread of the infective agent from human or animal host to man, (2) increase of specific or nonspecific resistance in the individual who may become exposed, (3) application of specific therapeutic measures to eliminate sources of spread of infection.

What are the chief sources of contamination of drinking-water?

Sewage emptied into the stream from which the supply is obtained; surface water in settled districts gaining entrance to the supply; subsoil water, after passing through infected soil; drainage from cemeteries and from soil containing mineral poisons; lead pipes.

Describe several methods of purifying drinking-water.

Sedimentation and storage allow suspended matter to settle, and pathogenic microorganisms are destroyed in the course of a month by the sun and predatory organisms (infusoria, etc.).

Copper sulfate added to the water destroys algae and prevents unpleasant odor and taste.

Oxidation by aeration to destroy algae, effected by projecting the water in a jet or spray, or having it fall in cascades.

Coagulation, by itself or in conjunction with sedimentation or sand filtration, to remove turbidity due to colloidal clay. The water is treated with sulfate of aluminum, which reacts with the alkaline carbonates to form aluminum hydrate.

Slow Sand Filtration: From a height of two to four feet, the water is projected into large filters, about an acre in extent, consisting of tiles covered with gravel and sand. Algae and protozoa growing in the sand form a biological film which destroys bacteria. From time to time the filters must be drained and cleaned by removing and washing the sand before it is replaced. Although the first cost is high, operating expenses are low. Bacterial removal of about 99 per cent is effected.

Disinfection with chloride applied as either liquid chlorine or a solution of bleaching powder (hypochlorite). Used as a finishing process after filtration or other methods of clarification.

Discuss purification of drinking-water in the home.

The best method is boiling the water from 15 to 20 minutes. Another is the addition of 1 teaspoonful of fresh chlorinated lime to 1 pint of water and adding this solution to the drinking-water in the proportion of 1 teaspoonful to 10 gallons, allowing it to act about 30 minutes. Domestic filters are not to be depended upon unless cleaned at least once daily, which is rarely done. They give a false sense of security.

What is the most sanitary way of disposing of city garbage?

Incineration.

What is the best sanitary plan for the disposal of sewage?

Collect the sewage in large tanks and add lime to it. Compress the solid material after its precipitation and incinerate. Allow the liquid sewage to flow upon specially prepared filter beds, which are subdrained; the water coming from these drains may then be allowed to flow into a stream without great danger of contamination.

State the advantages of cremation over earth burial.

The danger of contaminating the water supply in the vicinity of cemeteries is obviated, as all disease germs are completely destroyed.

What care should be employed in exhumations?

The exhumation of those dead of a contagious disease should be forbidden. Whenever possible, exhumation should be done in cold weather; the presence of all persons except those absolutely needed should be forbidden, and the coffin should not be opened, but placed at once in a zinc-lined box and sealed.

What do you understand by the "dry-earth system" as applied to excrementitious matter?

The discharges are received in a box containing dry earth, and, after the privy is used, fresh earth is added from a "hopper." The receptacle is emptied from time to time, and fresh earth placed in it.

Mention some of the objections to storage cisterns under ground. What are the objections to rain-water as a drink?

Storage cisterns are usually dirty, difficult to clean, and cannot be properly ventilated. The water in the cistern may be contaminated when the overflow pipe is connected with the drain or soil-pipe of a house.

Rain water is insipid; the first part collected contains dust, pollen, and other matters derived from the air.

What are the principal measures which you would employ for the prevention of the spread of infectious diseases?

Disinfection of all discharges and everything thas has come in direct contact with the patient. Soiled linen should be disinfected before being washed. The patient should have separate eating utensils. In the case of contagious diseases, *isolation* of the patient and nurse, who must not leave the sickroom without first cleansing hands and face with an antiseptic solution and removing the clothing worn while attending the patient. In the case of smallpox, strict isolation of both patient and nurse and quarantine of the entire household are necessary. To prevent the spread of a water-borne disease, all persons should be enjoined to drink only boiled water.

How may a privy in the city or country be kept from becoming a nuisance while in use?

A disinfectant and deodorant substance, such as chloride of lime, should be poured into the privy vault every few days, and the vault emptied at short intervals. Ventilation must be secured by means of a pipe extending from the vault to the top of the privy.

Mention some of the objections to curbed or driven wells in streets or houses, with respect to the purity of water coming from these wells.

The curbing rarely affords adequate protection of the well water against contamination from sewers and gas pipes. In driven, piped wells the water is taken from far below the surface, and in city streets the soil is so contaminated with noxious material that the water is in danger of pollution.

Name the principal animal-borne communicable diseases of man.

(1) Beef tapeworm, transmitted from cattle, (2) fish tapeworm, transmitted from fish, (3) pork tapeworm, transmitted from swine, (4) liver fluke, transmitted by fish, (5) schistosomiasis, transmitted by snails, (6) hydatid disease, transmitted by dogs, (7) Weil's disease, transmitted by rats, (8) psittacosis, transmitted by parrots, (9) ornithosis, transmitted by pigeons, (10) trichinosis, transmitted by swine, (11) tularemia, transmitted by rabbits, (12) lymphocytic choriomeningitis, transmitted by mice.

Mention some of the advantages of carefully prepared artificial ice as compared with natural ice.

If the proper precautions are observed in its manufacture, artificial ice is free from bacteria and inorganic impurities (lead, iron, etc.). The cakes may be frozen in any desired size and shape. Artificial ice plants can be established anywhere—in hospitals and other institutions—thus ensuring a constant supply of ice without dependence on local ice companies.

Through what media is the typhoid organism usually communicable?

Drinking-water; also milk, oysters, and green vegetables that are eaten raw. In each case it is the water in contact with these foods that has transmitted the bacteria.

Describe the transmission of diseases by meat and fish.

Diseases resulting from the eating of meat and fish may be due to (1) ptomaines or inorganic poisons, (2) vegetable parasites (bacteria), (3) animal parasites (worms or their larvae or ova) contained in the food.

Bacteria and animal parasites are destroyed by thorough cooking; poisons are not. "Measly" beef may contain the larva of *Taenia saginata,* or beef tapeworm, which develops into the adult worm in the human intestine. Beef is the *intermediate,* man the *definitive* host. In a similar manner, pork contains the larvae of *Trichinella spiralis,* and when eaten raw, especially in the form of sausage and Westphalia ham, or insufficiently cooked, may give rise to *trichiniasis* (trichinosis). The larvae enter the intestinal tract with the food; there they develop into adult worms, which in turn produce numbers of the larval worms and die. The larvae make their way into the muscles and become encysted.

What constitutes a thorough meat inspection?

Meat should be inspected within 24 hours after the animal has been killed. The following points are important: the quantity and character of the fat, its color, and consistency; the condition of the flesh and bone marrow; and signs of infectious disease in the lungs, liver, or kidneys. The flesh should be examined under the microscope for the presence of pathogenic bacteria, trichinae, or bladder worms (the larval form of tapeworms). When possible, it is advisable to investigate the methods employed in storage and refrigeration.

How should an inspection of milk be conducted?

The points for determination are: specific gravity, color, percentage of cream, presence or absence of preservatives, diluents, or coloring matter; quantity of total solids; quality and quantity of ash, fats, casein, and lactose. A bacteriological examination should be made and the number of bacteria noted. Finally, the source of supply and the methods of storing and distributing the product should be subjected to careful scrutiny.

Differentiate between endemic and epidemic diseases.

An endemic disease is one which is more or less constantly present in a certain district or locality. An epidemic disease is one that appears suddenly and attacks many persons at the same time.

List the principal insect-borne communicable diseases of man.

(1) Transmitted by mosquitoes: malaria, yellow fever, filariasis, dengue fever, and encephalomyelitis; (2) transmitted by flies: sleeping sickness and tularemia; (3) transmitted by ticks: Rocky Mountain spotted fever; (4) transmitted by lice:typhus fever; (5) transmitted by fleas: plague.

Give the incubation periods for the common communicable diseases.

(1) Chickenpox, 14 to 24 days; (2) German measles, 12 to 21 days; (3) measles, 10 to 15 days; (4) mumps, 12 to 26 days; (5) poliomyelitis, 5 to 21 days; (6) scarlet fever, 1 to 7 days; (7) whooping cough, 2 to 14 days.

Name the principal water-borne diseases.

(1) Amebic and bacillary dysentery, (2) typhoid and paratyphoid fevers, (3) cholera.

What are the principal adulterations of milk?

Addition of water and removal of cream; addition of coloring matter, preservatives (boric acid, salicylic acid, formalin), and gelatin for thickening.

Give 5 reasons why milk is responsible for more diseases than any other food.

(1) It is sometimes consumed in a raw state. (2) Milk affords a good culture medium for bacteria. (3) It decomposes readily. (4) It is difficult to handle in a clean manner. (5) It is obtained from animal sources.

Name six diseases that are communicable to man from milk.

(1) Typhoid fever, (2) tuberculosis, (3) diphtheria, (4) scarlet fever, (5) brucellosis, (6) septic sore throat.

Name 2 factors concerned with maintaining pure foods.

(1) Protection from dust, flies, rodents, and unnecessary human contact; (2) prevention of deterioration in transportation and marketing.

Name the various methods used in the preservation of food.

(1) Refrigeration, (2) drying, (3) salting, (4) smoking, (5) canning, (6) preserving, (7) chemical treatment, (8) fermentation, (9) sterilization by heat.

What precautions should a physician observe to avoid carrying contagious diseases?

Before entering the sick-room the physician should put on a gown long enough to cover the entire body, a cap to protect the hair, and a *mask* covering mouth and nose, leaving only hands and feet uncovered. Rubber gloves may be worn. In examining the patient, contact of any part of the body, except the hands, with the patient or bedclothes must be avoided. Immediately after leaving the sick-room, wash the face and hands thoroughly with soap and water and disinfect in carbolic acid or bichloride solution; then remove cap and gown. The nurse should be instructed to disinfect mask, cap, and gown with bichloride solution.

Discuss the etiology of diseases present at birth.

Diseases present at birth may be due to: (1) hereditary transmission—these diseases are limited to those transmitted through abnormalities of the genes in the chromosomes of the ovum or the sperm. The following conditions may be properly classified as being transmitted hereditarily: deaf-mutism, albinism, hemophilia (sex linked), brachydactylia and polydactylism, fragilitas ossium, cataract, retinitis pigmentosa, color blindness, allergy, migraine, Huntington's chorea, and Friedreich's ataxia. (2) Defects of development, such as harelip, cleft palate, spina bifida, and other anatomical anomalies, are usually attributed to circulatory or nutritional disturbances in utero affecting the growth and the development of the fetus. Likewise, congenital defects may be caused by intra-uterine infection, which may occur with syphilis, smallpox, measles, tuberculosis, and other diseases by transmission of the infectious agent through the placenta. There is conclusive evidence of a relationship between the occurrence of rubella in a pregnant mother and the occurrence of congenital defects in the infant. The risk of congenital defect in the infant increases when the infection occurs during the first two months of pregnancy (as high as 70 per cent) and decreases from the third month on. The occurrence of rubella in the first two months of pregnancy is considered by many to be an indication for therapeutic abortion.

Against what diseases may artificial immunity be acquired? How in each?

(*1*) *Smallpox:* By vaccination with the virus of cowpox or vaccinia.

(*2*) *Whooping cough:* Pertussis vaccine.

(*3*) *Diphtheria:* By the use of the toxoid or alum-precipitated toxoid, or toxin-antitoxin.

(*4*) *Typhoid* and *paratyphoid:* By the use of typhoid-paratyphoid vaccine in repeated and increasing doses.

(*5*) *Rabies:* Immunity may be produced after exposure by the use of rabies vaccine.

(*6*) *Cholera:* Vaccination against this disease is successful.

(*7*) *Scarlet fever:* Active immunity can be produced by vaccination with a suitable streptococcic toxin. Passive immunity by the use of human convalescent serum or scarlet fever antitoxin has been proved successful.

(*8*) *Tetanus:* Passive immunity by the use of 1500 units of antitoxin.

(*9*) *Measles:* Passive immunity by the use of human convalescent serum.

(*10*) *Mumps:* Passive immunity by the use of human convalescent serum, adult immune serum, and immune globulin.

(*11*) *Yellow Fever:* Passive immunity by the use of human convalescent serum. Active immunity by vaccination with an avirulent strain of living yellow fever virus.

(*12*) *Typhus Fever and Rocky Mountain Spotted Fever:* Partial immunity by vaccination with chemically killed rickettsiae.

(*13*) *Influenza:* Partial immunity by vaccination.

(*14*) *Poliomyelitis:* The Salk vaccine is approximately 85 per cent effective.

Outline the schedule for poliomyelitis vaccination (Salk).

Although young children are most susceptible to the disease, it infects adults, including those over age 40. All pregnant women should be immunized because there is a higher than average incidence of poliomyelitis among nonimmunized women during pregnancy and after delivery. Babies of mothers thus protected usually have a satisfactory antibody titer for the early months of life. The American Academy of Pediatrics recommends the following schedule: Infants: Begin at 2 months of age: 3 injections at monthly intervals, combined with DPT; subsequent booster 7 to 12 months later combined with DPT; and subsequent boosters combined with DPT or DT at 4-year intervals. Older children and adults: Two successive doses 1 month apart, followed by a third injection after 7 months; booster 12 months after third injection and subsequent booster inoculations as indicated.

Discuss the limitations of poliomyelitis vaccine (Salk).

(1) Persons who have agammaglobulinemia may not be capable of making a favorable immune antibody response to any vaccine, and (2), since several weeks are needed for a favorable degree of immune antibody reaction, the vaccine cannot be expected to protect if it is given after the beginning of the incubation period.

Discuss oral poliomyelitis vaccine (Sabin).

The advocates of the oral attenuated live-virus vaccine believe that it can kill the unattenuated viruses of poliomyelitis and eliminate breeding in the human intestine. Others state that the Coxsackie, enteroviruses, and naturally occurring poliomyelitis viruses may interfere with such an effect. At this time there have not been enough controlled studies of oral live attenuated vaccines completed to prove its relative effectiveness as compared to killed virus vaccine (Salk). However, preliminary reports suggest that oral vaccine is safe and gives better and longer protection.

List the complications of and name one contraindication for smallpox vaccination.

Complications: erythema multiforme, eczema vaccinatum, generalized vaccina, vaccina necrosum, postvaccination encephalitis.

Contraindication: a generalized skin disease with open lesions—as eczema.

Give the accepted practice in regard to revaccination.

Children who have been vaccinated in the first year of life are customarily revaccinated when they enter school. Two successful vaccinations are believed to confer a practically permanent immunity. Colleges, hospitals, and other institutions usually require a certificate of successful vaccination or revaccination before admission. Persons about to visit countries where sanitation is faulty, as missionaries and the like, should be vaccinated in any case. The same applies to the population generally in the presence of a smallpox epidemic.

What is the best method of disposing of the bodies of those who have died of yellow fever?

Cremation.

What is plague? What steps can be taken to limit or extinguish such a scourge?

An acute specific infection caused by *Pasteurella pestis,* the plague bacillus. The *bubonic* form is characterized by inflammation and suppuration of the lymph nodes, especially in the groin (hence the name). The *pneumonic* form is a rapidly fatal pneumonia with terminal septicemia. Rats play the capital role in dissemination of the plague; but other small rodents, in California notably the ground squirrels and chipmunks, are also a source of infection. Pneumonic plague is also transmitted directly from man to man. The "vectors" in the transmission of the bacillus are the rat flea and other species of parasites that infest rodents.

Prevention: Strict isolation of patients and protection of attendants by masks, gowns, and gloves. Contacts to be quarantined for seven days. Active immunization with Haffkine's vaccine affords some protection, as does also passive immunization with Yersin's serum. One attack confers immunity, which is usually permanent. Although complete extermination is impossible, rats and other rodents must be destroyed by all possible means—fumigation of holes and burrows, trapping, poisoned bait, etc.

Discuss the value of vaccination against salmonellosis.

Protection against salmonellosis by vaccination is only relative and under conditions of heavy exposure infections may occur despite immunization. However, the marked decrease in infections caused by *S. typhosa* is related in part to the widespread use of typhoid vaccine. Since the vaccine commonly used in this country contains only *S. typhosa, S. paratyphi,* and *S. schottmülleri* (typhoid-paratyphoid A and B bacilli) and affords no protective immunization against Group C salmonellae, this may explain in part the comparatively high incidence of infections caused by members of this group.

What specific prophylactic measures are available against scarlet fever?

Both a toxin and an antitoxin have been used for immunization of individuals shown to be susceptible by a preliminary Dick test. Passive immunity lasting 4 to 8 weeks is obtained by administering 1,000 to 8,000 units of the antitoxin intramuscularly. Active immunity lasting about 3 years may be produced by giving 3 to 5 doses of the toxin at weekly intervals. The value of active immunity is widely debated.

Alum-precipitated toxoid is preferable to toxin-antitoxin because of absence of serum sensitivity with the former. The toxoid is given subcutaneously in doses of 0.5, 1.0, and 1.5 cc. at monthly intervals.

What is the significance of the Schick test? Describe the test briefly.

A positive reaction indicates that the individual is susceptible to diphtheria and should be given an immunizing injection of antitoxin-toxin mixture. A negative reaction is a sign of immunity.

The *test* consists in injecting intracutaneously one fiftieth of the minimum lethal dose of toxin in 0.1 to 0.2 cc. of saline solution. A 1-cc. syringe with a short 26-gauge needle is useful.

Discuss the value of antibody prophylaxis in (1) rubeola (measles), and (2) rubella (German measles).

The administration of convalescent serum or gamma-globulin during the period of incubation may prevent or modify the manifestations of rubeola. For rubella, antibody prophylaxis has for the most part been disappointing. Nevertheless, women exposed to rubella in early pregnancy should receive the benefit of gamma-globulin prophylaxis despite its ambiguous status.

Discuss briefly immunization as prophylaxis for tetanus.

Immunization can be achieved by the use of antitoxin, toxoid, or a combination of both.

Antitoxin: If a patient is seen within 24 hours after a wound has been received, 1,500 units of antitoxin should be given. With large wounds, gross contamination, diabetes mellitus, or decrease in arterial blood to the area of the wound, 3,000 units of antitoxin should be given. If seen after 24 hours the dosage of toxoid should be doubled for each day elapsing between the time of the wound and the time of treatment, up to 10,000 units. Surgical débridement should be done whenever possible. Wounds remaining unhealed over longer periods of time require an additional 1,500 units every 7 days until the wound is clean or healed, or 100,000 units initially will give protection for 3 weeks. All patients who are to receive antitoxin must have intracutaneous and ophthalmic tests for sensitivity to horse protein. The antitoxin is diluted 1:10 with saline and 0.05 cc. should be dropped into the conjunctival sac of the eye or given intracutaneously. Negative results of these tests do not completely exclude fatal anaphylactic reactions; nor do these tests rule out delayed serum reactions which occur within 10 days. Intrathecal or intravenous injection of serum is more hazardous than intramuscular injection. If the skin test is positive, or the patient has a known sensitivity to horse serum, or he has received previous doses of antitoxin which suggest that serum therapy is dangerous, an antitoxin prepared from cows may be used after skin testing with the bovine serum. The injection of 0.3 ml. of 1:1000 adrenalin in oil, or antihistamine drugs for 10 days, are helpful for the prophylaxis of serum sickness. ACTH has been helpful in the treatment of severe reactions.

Toxoid: Initial vaccination with alum-precipitated toxoid can be obtained with 3 monthly injections and a fourth dose 6 to 12 months later. Booster doses should be of fluid toxoid at 4-year intervals or after any injury. After 4 years it may require 6 or more days for response to toxoid and during this interval the patient should be protected by antitoxin.

Antitoxin and Toxoid: In addition to these situations, patients not previously vaccinated with toxoid should preferably receive antitoxin and toxoid at different sites at the time of injury.

Discuss chemoprophylaxis of infectious diseases.

In general, prophylactic antimicrobial therapy has been used primarily for four purposes: (1) To protect healthy people, either singly or in groups, against infection by specific microorganisms which they may or may not always be harboring. This type of chemoprophylaxis has been most successful in protecting against infection by the beta hemolytic streptococcus, gonococcus, meningococcus, and the dysentery bacilli. (2) Prophylaxis is used for the prevention of bacterial invasion in patients taken suddenly ill with disorders in which these drugs have no therapeutic effect, namely, virus diseases and diseases of noninfectious origin. This type of prophylaxis is of questionable value. (3) Chemoprophylaxis is employed successfully in patients suffering with chronic illnesses. It is used for the prevention of subacute bacterial endocarditis in persons with congenital or acquired heart disease in which certain operative procedures are performed, and to prevent recurrence of rheumatic fever. (4) The prophylactic use of these agents in the field of surgery. Although no one questions the use of the antimicrobial agents for the prevention of invasive infection in the infected case, there is reason to question the advisability of employing these drugs routinely in clean cases, in the hope of preventing a postoperative infection. It would seem best to withhold all antimicrobial therapy until a complicating infection develops and then institute the drug, or drugs, of choice.

Outline prophylaxis against the recurrence of rheumatic fever.

Patients in the inactive phase should receive 200,000 to 300,000 units of penicillin by mouth each morning before breakfast, or 600,000 to 1,200,000 units benzathine penicillin G intramuscularly every 2 to 4 weeks. This is continued throughout the year and for children until age 20. All others should receive the same for at least 4 years. Individuals sensitized to penicillin may be given sulfadiazine 0.5 gm. to 1.0 gm. orally each day. If respiratory infection occurs, throat cultures should be taken and penicillin, 600,0000 units intramuscularly daily, should be given. If cultures are positive for group A hemolytic streptococci, penicillin should be continued for 10 days.

What is the value of the tuberculin test?

The Mantoux intracutaneous test is a reliable study for the exclusion of tuberculosis. Tuberculin, 0.1 cc., containing either 0.1 mg. O.T. (old tuberculin) or 0.0001 mg. of P.P.D. (purified protein derivative), may be given and, if no reaction occurs, this can be repeated after an interval of 4 to 5 days, using 10 times the original concentration. The only significant exception is that patients in the terminal stages of tuberculosis often become anergic.

All patients with chronic pulmonary disease in which bacteriological proof of the diagnosis is not obtained should have a tuberculin test. Less than half the population now have positive tuberculin reactions, and the percentage of reactors diminishes each year. Thus there is a considerable likelihood, even in urban adults, of finding a negative tuberculin test and thereby securing strong evidence that the disease in question is not tuberculosis. The tuberculin test is also useful when given other members of the patient's family, not only indicating those who need x-ray examination, but serving also to indicate whether the patient has been infectious.

What is the management of a patient found in an x-ray survey to have pulmonary abnormalities suggestive of minimal tuberculosis?

A 14- by 17-inch x-ray film of the chest or, if possible, stereoscopic films, should be made to determine more accurately the appearance of the lesion. Thorough clinical examination may disclose symptoms or signs suggestive of tuberculosis or may reveal evidence indicative of some other disease, such as pneumoconiosis or bronchiectasis. Sputum, if available, should be repeatedly searched for tubercle bacilli. If negative, a tuberculin test should be made. If a positive reaction is found, at least three gastric lavages should be performed and the material cultured or inoculated into guinea pigs. If the tuberculin test is negative, other skin tests as indicated by the residence history may be required, e.g., coccidioidin or histoplasmin tests. Bronchoscopy should be done if the patient is an adult and if the clinical study or x-ray films are at all suggestive of neoplasm.

The decision of whether the patient may continue at work or should be hospitalized pending the outcome of bacteriological study, must be based on a judicious appraisal of the clinical and x-ray findings. Even when bacteriological proof is not forthcoming, it is sometimes justifiable to admit a patient to a sanatorium if the roentgenological appearance of the lesion is typical of a fresh tuberculous infiltration.

What rules in public health administration should be promulgated to prevent the spread of pulmonary tuberculosis?

Expectoration on sidewalks and on the floors of all public places and public conveyances should be prohibited. Houses that have been inhabited by tuberculous inmates should be disinfected. All tuberculous cattle should be condemned and killed. Persons suffering from tuberculosis should not be allowed to prepare or distribute food.

How should a room recently occupied by a person suffering with tuberculosis be disinfected?

The room should be closed hermetically and thoroughly disinfected with formalin, after which the walls should be repapered or painted.

State the best means of sputum disposal.

The sputum should be received in a paper spit cup, set in a metal box with a lid. The spit cup is taken out of the container, burned, and another put in its place.

Define the term "quarantine," and mention the principal quarantinable diseases.

The adoption of measures to prevent the introduction of disease from one country or locality into another. The word originally meant isolation for forty days (*quaranta,* Italian, "forty").

The principal quaratinable diseases are: cholera, smallpox, yellow fever, scarlet fever, typhus fever, diphtheria, poliomyelitis, and cerebrospinal fever.

Give a medical and hygienic plan for the inspection of immigrants who have just arrived at a seaport.

First examine the "bill of health" and the records of all cases treated during the voyage, as well as the list of passengers and crew. Then examine the entire ship's company for transmissible disease. If a case of infectious disease occurred during the voyage, disinfect all freight and clothing that has been exposed to the infection, and detain all the persons who have been exposed until the period of incubation of the disease has passed.

Describe external cardiac massage.

Sustained ventricular standstill is incompatible with life and, when it strikes prematurely, prompt action is required. When the heart stops on the operating table or in any well-equipped hospital, open-chest massage of the heart is possible. However, many of these catastrophies do not occur in a hospital and so many lives are lost. Recently, it has been demonstrated that one can effect cardiac massage by rhythmically pressing on the xiphoid with the heel of the hand. The technique can be expected to maintain only a marginal cardiac output until some definitive measure can be taken to restore normal heart action. However, it has also been demonstrated that a heavy hand on a frail chest is not without risk, in that overenthusiastic external cardiac massage can fracture ribs and lacerate the liver. Hence, if the police, firefighters, etc., are to be instructed in the use of this technique, they must also be taught when to use it as well as how to use it. Otherwise, those who are apt to faint in public places may suffer cracked ribs and torn livers for their indiscretion.

What diseases are incident to school life? How may these diseases be prevented?

The communicable diseases, nutritional and nervous disorders, anemia, eye-strain and refractive errors, eye and ear infections (conjunctivitis, trachoma), diseased tonsils and enlarged adenoids, parasitic skin diseases (ringworm, favus, scabies, impetigo), curvature of the spine and other orthopedic deformities.

The infectious and parasitic diseases may be prevented by early recognition and prompt removal of the affected pupils. For this purpose systematic *school inspection* is necessary. Curvature of the spine may be prevented by using properly constructed school furniture, disposed in such a way as to secure the best illumination, and by teaching the children to hold themselves properly when reading and writing. The same measures, with the additional precaution of using textbooks with clear, large print, will combat the progression of myopia and other refractive errors. The light in a schoolroom should come from above. The windows should extend to the ceiling and the window sills be above the level of the pupils' eyes when they are seated. The upper part of the walls and window shades should be of a light color (white, light yellow, or green), the lower parts of a darker shade. Blackboards, maps, and charts, which should have a dull finish, must be so placed as not to reflect the light into the pupils' eyes. Plenty of outdoor exercise and a substantial hot lunch in the middle of the day minimize the incidence of nutritional and nervous disorders.

Give the sanitary dimensions of a schoolroom for fifty pupils.

A room 40 feet long, 25 feet wide, and 15 feet high would give each pupil 300 cubic feet (8.5 cubic meters) of air space, which, with good ventilation, is adequate for each child.

How much fresh air is required by an adult for normal respiration during twenty-four hours?

3,000 cubic feet per hour, or 72,000 cubic feet in 24 hours.

What deleterious gases accumulate in improperly ventilated sleeping-rooms?

Carbon monoxide, carbon dioxide, hydrogen sulfide, and ammonium sulfide.

Why and how is carbon dioxide deleterious to health?

In itself it is not injurious in ordinary proportions, from 0.03 per cent in pure open air to 0.6 or even 1 per cent in closed rooms; 2 to 3 per cent causes increased respiration; 7 to 8 per cent, dyspnea; 30 per cent, suffocation. Carbon dioxide is an indicator of the quantity of inorganic impurities present. A larger proportion of artificially prepared CO_2 can be tolerated than of CO_2 resulting from rebreathing (vitiation). It cannot be taken as a guide to the fitness of air for breathing, which must be determined by temperature, humidity, and motion of the air.

What are the necessary hygienic conditions of a model sleeping-room?

The height of the apartment should be 9 feet, the floor space 16 square yards; 25 cubic yards of air space must be allowed for each occupant. The temperature in winter should not be above 68°F. The room must have at least one window, equal in area to at least one tenth of the floor space, and opening half its size.

What is the proper temperature for a living-room in winter?

68° to 70°F.

Describe a simple method of ventilating the sick-room.

In winter place a wooden strip, 3 inches wide and as long as the window frame is wide, under the lower sash; through the space between the top of the lower and the bottom of the upper sash, enough air will enter the room. In summer open the windows from the top. Be careful that the patient is protected from drafts.

Discuss the different methods of heating houses.

The *hot-water system* is the cleanest, simplest, and most efficient, but has the drawback of not providing ventilation unless indirect radiation is employed. (Radiation is *direct* when the radiators are placed inside the rooms, *indirect* when the heated air enters through flues from radiators placed outside.) Provision must also be made for humidifying the air.

Steam heating is more efficient for large installations, but less desirable from the standpoint of controlling the degree of heat, the inconvenience of steam pipes, and the necessity for constant supervision of the boiler. Ventilation and humidification the same as with hot-water heating.

Hot-air heating has the advantage of bringing in a continuous supply of fresh air and gives better humidification than hot water or steam. Disadvantages are: street dirt and dust are brought in with the air intake, necessitating filtering; this is sometimes obviated by drawing the air supply from inside the house (also more economical of fuel) at the sacrifice of ventilation, however. The furnace in time becomes leaky and coal gas escapes into the rooms. The system is also more expensive as to installation, maintenance, and fuel.

Open fireplaces supply a very irregular heat, cause drafts, and are exceedingly wasteful in fuel, besides requiring constant attention. Individual stoves are more efficient since they can be placed in the middle of the room.

Give the special hygiene of factories.

Sufficient air space must be allowed for each person employed to ensure a supply of from 60 to 100 cubic meters (about 2,000 to 3,500 cubic feet) of fresh air per hour. Thus, if the ventilation is such that the air is renewed 3 times in an hour, the amount of air space per individual must be from 20 to 35 cubic meters (about 700 to 1,200 cubic feet). Suitable exhaust ventilators that will carry off dust as well as vitiated air and injurious gases must be installed. The temperature should be about 65°F. Ample and properly constructed washrooms and water closets with modern plumbing must be provided.

Discuss detached wards versus many-storied buildings for a public hospital.

General supervision and discipline are easier in hospitals consisting of one large building. Other advantages are ease of communication, prompt service, and economy of administration. On the other hand, the isolation of suspected or contagious cases is more difficult (the roof can be utilized for an isolation ward, as in some modern hospitals), the supply of sunlight is less, and the danger in case of fire greater.

Discuss the prevention of malaria.

Malaria is transmitted by the anopheline species of mosquito after it has bitten an infected human being. Hence, prevention consists in protection of both patients and the population generally against mosquitoes by screening and measures to exterminate mosquitoes. Whenever feasible, all ponds, stagnant pools, and other breeding places are drained or filled. If this is not possible, the water is treated with oil or other larvicide, or, in the case of streams and ponds, they may be stocked with minnows. Multiplication of the plasmodia in the blood of infected persons is combated by the continuous administration of quinine or other antimalarial remedies, preferably chloroquine (Aralen) or proguanil (Paludrine).

What single factor has been responsible for the reduction of death rate from puerperal sepsis and which measures should further reduce it?

(1) The introduction of the sulfonamides and penicillin. (2) Improved antepartum and adequate postpartum care.

Name the diseases responsible for most intrauterine infections.

Syphilis and measles are the most common, but malaria, smallpox, and typhoid fever may also be transmitted to the fetus from the infected mother.

List the precautions concerning the sanitation of swimming pools.

(1) Bathers must shower with soap before entering pool. (2) Adequate toilet facilities should be available. (3) Towels and bathing suits should be sterilized after use. (4) The purity of the water should be equal to that of good drinking water and should be maintained by filtration and disinfection—10 per cent of fresh water every day and frequent bacteriological examinations. (5) The pool should contain at least 400 gallons of water per bather and should be thoroughly cleaned at frequent intervals.

What factors influence the effectiveness of protective clothing against cold?

(1) Even distribution of insulation—local cooling occurs at poorly insulated areas. (2) Accumulation of sweat, which markedly reduces insulation. (3) Body work, for movement increases loss of heat by convection.

Discuss the problem of hospital-acquired infections.

It is now evident that strains of staphylococci recovered from patients in a hospital and from hospital personnel possess considerable resistance to most of the antibiotics, whereas a high percentage of strains recovered from persons outside a hospital are susceptible to the action of these agents. The incidence of antibiotic resistance of strains is roughly proportional to the quantity of an antibiotic used in a hospital. These resistant strains, which are carried by patients and hospital personnel, infect wounds and cause pneumonia, enteritis, genitourinary-tract infections, and septicemia. Thus, patients go into hospitals to be cured, but some acquire infections that may seriously impair their health, as well as prolong their stay in the hospital and thereby increase the bed shortage.

In general, those patients with advanced, serious, and potentially fatal disease represent the population group which acquires staphylococcal infections within the hospital. It appears that the healthy human host possesses a high degree of resistance to such infections. Thus, it is difficult to assign therapeutic failures to drug resistance alone in a significant number of cases, in that the basic underlying disease upon which staphylococcal infection is superimposed is commonly the important factor in determining the outcome. Furthermore, despite the inclusion of staphylococci with other microorganisms producing acute infections in man, it is clear that there are unique features in staphylococcus-host relationships which set this microorganism apart as a highly adaptable parasite, capable of surviving within human serum and phagocytic cells, and adjusting to meet unfavorable new environments, including human tissues bathed in antimicrobials. Also, it appears probable that staphylococcal infections, once initiated, will continue to cause the death of a number of seriously ill patients who now constitute a large part of our hospital populations.

As noted above, the staphylococci are the prime offenders, but strains of *Escherichia coli,* associated with infantile gastroenteritis, are also suspect, and hemolytic streptococci may be protected by fellow-travelling penicillinase-producing staphylococci. These resistant strains are developed in patients and are stored in various sites. Such reservoirs of infection include: the tainted thermometer, bathtubs, mattresses, blankets, pillows, the nurse's hands, her dress, and her "droplets"—in fact, practically everything may be contaminated. Thus, it is apparent that the prevention of secondary infections in a hospital is an exceedingly difficult task. Although they cannot be entirely eliminated, much can be done to reduce their incidence.

From these observations, it is apparent that the progressive emergence and spread of antibiotic-resistant staphylococci is something more than a bacteriologist's "bogey." Certainly the practicing physician must give constant and careful attention to this problem, or infections due to the staphylococcus acquired in hospitals will increase. This problem cannot be solved by dosing the patients with antimicrobial agents, as this procedure merely aggravates the situation by facilitating the development of antibiotic-resistant organisms. Also, it is doubtful that new antimicrobials will alter this situation unless they are specifically and highly active against staphylococci and provided that the infections are recognized and treated early. However, there is much to suggest that antimicrobials have played a role in the emergence of staphylococci as a serious hospital problem and additional agents may make man's battle against the staphylococci more difficult. Thus, the first line of defense is to block the channels of transmission of the pathogens, with antibiotics used only to treat the established infections and only in those in whom other methods fail. Certainly the prophylactic administration of antimicrobial agents as a routine procedure before and after all operations may be more harmful than beneficial and is therefore not advisable. Nurses and doctors should wear sterile rubber gloves, efficient masks, and efficient sterile overalls. Open wounds should be dressed in a dressing room and not on a ward. Unsterilized blankets, soiled dressings, and casts should be removed before the patient is wheeled into the operating or dressing room. In preparing a patient for operation, the site of the incision should be properly cleansed. Proper ventilating systems should be present in operating and dressing rooms to carry particles out toward the floor. Mattresses, blankets, cups, etc., should be thoroughly sterilized. A vacuum cleaner should be used on the floors, rather than sweeping with a broom, regardless of whether oil is used or not. These and similar measures have already proved effective in decreasing the incidence of hospital-acquired infections.

Discuss the control of ionizing radiation.

The public-health approach to radioactive hazards should include: (1) maximum control of ionizing radiation from such sources as radium and x-ray machines; (2) adequate protection of the population from hazards related to nuclear reactors used to produce power; and (3) proper disposal of radioactive wastes by infinite dilution in the ocean, by storage with adequate shielding protection, or by more effective methods that must still be developed.

Section 8

SURGERY

INFLAMMATION AND WOUNDS

What are the causes of inflammation?

The chief causes are of mechanical, chemical, thermal, bacterial, or traumatic origin. Predisposing causes include both (*a*) local and (*b*) systemic factors: i.e., (*a*) devitalized tissue, blood supply, foreign material, repeated exposure to one or more of the aforementioned causes, or (*b*) age, nutrition, or lack of leukocyte or specific antibody response.

How does a carbuncle differ from a furuncle?

A *carbuncle* is a localized inflammation of the skin and subcutaneous tissue, with greater necrosis and greater suppuration than a furuncle and with multiple openings through the skin. It differs from a *boil;* it is much larger, flatter, and less conical, is accompanied by extensive edema of the surrounding tissues, and larger sloughs are discharged through multiple openings. A *furuncle* is a small abscess resulting from infection of the gland ducts or hair follicles of the skin.

Define septicemia and give its symptoms.

Septicemia is a septic intoxication caused by the absorption of bacteria or bacterial products into the blood.

Symptoms are irregular temperature ranging from 100° to 105°F., weak and rapid pulse, frequent chills, sweats, severe headache, nausea, often vomiting and diarrhea. Culture of the blood may show the presence of the etiological organism.

Define peritonitis. State three ways in which the peritoneum may be inoculated by bacteria.

Peritonitis is inflammation of the peritoneum from any cause. Bacteria may reach the peritoneal cavity: (1) by means of an abdominal wound or the entrance of a foreign body; (2) by extravasations from the stomach, intestines, gallbladder, urinary bladder, uterine tubes, or uterus, or by the passage of microorganisms through the damaged walls of any of these viscera, or by rupture of an abscess of the pancreas, spleen, or liver; (3) by way of an open uterine tube.

Define anthrax (malignant pustule) and give its etiology and treatment.

Malignant pustule or "woolsorters' disease" is a local lesion produced by infection with *Bacillus anthracis*. It differs from an ordinary carbuncle in the following respects: the presence of a central, depressed, blackish slough; absence of localized pain; absence of suppuration (unless mixed infection is present); greater severity of the constitutional symptoms. Occasionally, a severe type of pneumonia, due to inhalation of spores, occurs.

Treatment: All surgical intervention should be avoided. Cauterization, incision, and excision accomplish nothing and increase the mortality. Isolate the wound. Penicillin and broad-spectrum antibiotics have replaced treatment with anthrax antiserum.

What prophylactic treatment should be given for gas gangrene?

Adequate debridement and treatment of the wound by delayed closure after it is clean. Antitoxin is ineffectual prophylactically, and toxoid for gas gangrene is in the experimental stage.

TREATMENT OF WOUNDS

How are wounds classified?

Incised, lacerated, contused, abrasive, punctured, poisoned, and gunshot. They may also be designated as clean, infected, or contaminated. Wounds in the vicinity of great serous cavities are divided into penetrating and nonpenetrating types.

What factors influence the efficiency of the healing process?

(1) State of nutrition: vitamin C is essential for proper collagen formation; proper healing of bone is promoted by a sufficiency of vitamins C and D; adequate proteins, since wound healing is delayed when plasma proteins are reduced. (2) The wound must have complete protection from any sort of bacterial, mechanical, or chemical irritant. (3) Experimentally, administration of cortisone or ACTH, which appears to depress formation of granulation tissue and delay wound healing.

What are the types of wound healing?

There are three types: first intention, second intention, third intention. Healing by first intention is illustrated by a clean wound with edges accurately approximated and granulation tissue growing over the small crevice between the cut edges. Healing by second intention is illustrated by the granulation and epithelialization of a gaping wound that heals without suturing. Healing by third intention is illustrated by a wound that heals after delayed primary or secondary suture.

Describe the steps in the treatment of a scalp wound.

Hemorrhage is to be controlled by pressure or ligation. The scalp should be shaved for a distance of several inches from the margins of the wound. All foreign substances are removed and the wound is cleansed by irrigating with sterile saline solution. All scalp wounds should be explored with a gloved finger for foreign body or fracture. After closure a dry sterile dressing is applied. If the wound subsequently shows signs of infection, one or more of the sutures should be immediately removed, the wound again cleansed, packed with gauze, and allowed to granulate. Antibiotics, tetanus antitoxin or toxoid, and gas-gangrene prophylaxis should be given when indicated.

LIGATIONS

What are the indications for ligation of the lingual artery? Give the steps of the operation, omitting aseptic details.

The lingual artery is most frequently tied as a preliminary procedure to removal of the tongue. Other indications for its ligation are to check the growth of advanced carcinoma of the tongue and to control hemorrhage from the artery or its branches when they cannot be controlled by pressure.

Operation: The patient should be on his back, his shoulders raised, and the head extended and turned to the opposite side. Starting just below the symphysis of the jaw, an incision is made which passes downward and outward to the greater cornua of the hyoid bone, and then upward to the angle of the jaw. This incision divides the skin and both layers of the superficial fascia with the inclosed platysma and exposes a portion of the submaxillary gland. The deep fascia covering the gland is now incised, and the gland loosened and held up by a retractor. *Lesser's triangle,* formed by the two bellies of the digastric muscle below and the hypoglossal nerve above, is now exposed. The floor of this triangle is formed by the hypoglossus muscle. The stylohyoid and the tendon of the digastric are drawn downward, the lingual vein and the hypoglossal nerve upward, and an incision is carefully made through the hypoglossus muscle just above the hyoid bone. An aneurysm needle armed with a ligature is now passed about the artery, the ligature tied, and the external wound sutured.

The artery may also be ligated before it passes beneath the hypoglossus muscle.

Describe the operation for ligation of the subclavian artery in its third portion.

The patient should be in the dorsal position, with a cushion beneath the shoulders, the face turned to the opposite side. The skin should be drawn down over the clavicle, and an incision made over the bone extending from the anterior border of the trapezius to the posterior border of the sternomastoid. The skin is then allowed to retract, after which the wound will be ½ inch above the clavicle. This incision divides the skin, superficial fascia, platysma myoides, and the superficial layer of the deep fascia. If this does not give enough room, the clavicular head of the sternomastoid is divided. The prevertebral fascia is then incised, and the anterior scalene muscle located by its attachment to the scalene tubercle on the first rib and retracted inward. The phrenic nerve is situated on its upper surface. Care must be taken not to wound the subclavian vein or the pleura. The artery is located to the outer side of the scalene tubercle. The ligature is passed from before backward and from below upward.

How would you expose the brachial artery for ligation in the middle of the arm?

With the arm abducted to a right angle, make an incision 3 inches long in the middle of the arm, in the direction of a line extending from the middle of the clavicle to the middle of the bend of the elbow. Incise the skin and superficial and deep fascia. Locate the inner edge of the biceps, retract it outward bringing the median nerve into view, and retract this outward. The artery can then be visualized and ligated.

Give the indications and methods for ligation of the common carotid artery.

The artery is ligated for aneurysm which cannot be replaced by grafts; for wounds of the artery; and, rarely, to control the growth of malignant tumors.

Ligation in the Superior Carotid Triangle: The patient should be on his back with his shoulders elevated, the head thrown back, and the face turned slightly to the opposite side. An incision 3 inches long is made in the line of the artery (from the sternoclavicular articulation to a point midway between the angle of the jaw and the mastoid process), the center of the incision being opposite the cricoid cartilage. The skin, superficial fascia, platysma, and superficial layer of the deep fascia are divided, the sternomastoid muscle drawn outward, the tendon of the omohyoid drawn downward, and the pulsation of the artery sought for beneath the sternomastoid. The sheath is now opened, a threaded aneurysm needle is passed from without inward, the ligature grasped, and the needle withdrawn.

Ligation in the Inferior Carotid Triangle: The incision is made in the line of the artery from the level of the cricoid cartilage to the sternoclavicular articulation. The remainder of the operation is the same as the above, except that the omohyoid muscle is retracted upward.

Describe the ligation of the femoral artery at any selected point.

Ligation at the Apex of Scarpa's Triangle: The line of the artery is from a point midway between the anterior superior spine of the ilium and the spine of the pubis to the adductor tubercle on the inner condyle of the femur. An incision is commenced 3 inches below Poupart's ligament and carried downward for about 3 inches in the line of the artery, dividing the skin, superficial fascia, and fascia lata. If the lymph nodes are exposed, they may be held to one side or removed. In making the incision the internal saphenous vein should not be wounded. The sartorius muscle should now be located. The artery will be found beneath this muscle.

Describe the anastomosis which takes place after ligation of the femoral artery at its middle third.

The profunda femoris anastomoses with the articular branches of the popliteal and anastomotica magna; the comes nervi ischiadici with the branches of the popliteal; the circumflex with the articular branches of the popliteal and anastomotica magna.

What arteries need ligating in amputation at the middle third of the leg? Describe a method of ligating.

The anterior and the posterior tibial and the peroneal. Grasp the vessel with a hemostat and free it from the surrounding tissues; pass a ligature around the vessel and tie one knot; then take off the hemostat, tighten the ligature, and tie the second knot. Place a second transfixing ligature just distal to the first ligature.

Describe the anastomosis which takes place after ligation of the third part of the subclavian artery.

The transverse scapular, the descending branch of the transverse cervical, and both branches of the subclavian anastomose with the subscapular of the axillary; the internal mammary anastomoses with the highest intercostal, lateral thoracic, and branches of the subscapular; and small vessels from branches of the subclavian anastomose with small vessels of the axillary below.

DISEASES OF BLOOD VESSELS

What are methods of controlling hemorrhage?

Direct pressure; cold or hot water; elevation; styptics; cauterization; acupressure; suture; torsion; ligation; and hemostatic agents, such as fibrin foam, oxidized cellulose, and gelatin sponge, with or without thrombin; or the replacement of specific clotting factors may be effective in controlling hemorrhage.

Describe intermediate and secondary hemorrhage, giving both the preventive and curative treatment of each.

Intermediate Hemorrhage: This is defined as hemorrhage that recurs within forty-eight hours of an operation or accident.

PREVENTIVE TREATMENT: The ligatures should be properly tied so as to include the isolated artery and not the surrounding tissues. All bleeding points should be carefully and completely controlled at the time of injury or operation.

CURATIVE TREATMENT: Elevation and pressure may suffice. If these measures are not successful, the wound should be reopened, irrigated with hot salt solution, and all bleeding points tied. If ligatures cannot be applied, resort to hemostatic agents, or cautery, or pack the wound with gauze.

Secondary Hemorrhage: This is defined as any hemorrhage occurring in a wound after the lapse of 48 hours.

PREVENTIVE TREATMENT: Employ thorough asepsis and prevent infection. Carefully apply ligatures to all bleeding points. Use irradiation cautiously when tumor tissue infiltrates the walls of vessels.

CURATIVE TREATMENT: Determine whether the hemorrhage comes from the end of a divided artery or from an artery that has been ligated in continuity. If the hemorrhage comes from the end of an artery, first elevate the part and apply pressure. If the bleeding does not stop, open the wound and ligate the artery; if this is not possible, apply hemostatic agents, i.e., fibrin foam, oxidized cellulose, or gelatin sponge with or without thrombin. It may be necessary to pack the wound with gauze. If the hemorrhage comes from an artery that has been ligated in continuity, the same local treatment should be adopted. If this is unsuccessful, ligate the vessel proximally. Replace blood loss by transfusion of whole blood.

How can hemorrhage from the liver be controlled?

Ligate bleeding vessels, if possible, or place deep mattress sutures in the liver parenchyma. If the hemorrhage is still uncontrolled, apply fibrin foam, oxidized cellulose, or gelatin sponge with or without thrombin; pack with gauze, or apply a portion of skeletal muscle to the bleeding area; or use cauterization.

Describe the following types of sutures: interrupted, continued, delayed primary, and secondary.

The *interrupted* suture consists of a number of single stitches, each one being independent of the next. In a *continued* suture, the suture traverses the wound continuously in the same direction, being tied only at the beginning and at the end. A delayed primary suture is one that is placed after operation but before granulation tissue appears in the wound. A secondary suture is one that is placed at some time after granulation tissue appears.

What blood vessels may be involved in severe epistaxis? Describe methods of controlling severe epistaxis.

The venous plexus on the lower, anterior portion of the septum; rarely, the anterior septal artery; occasionally an anomalous artery or vein. (1) Pack the anterior naris with pledgets of absorbent cotton saturated with thrombin solution, fibrin foam, oxidized cellulose, or gelatin sponge with or without thrombin. (2) Pack the posterior naris after the method of Bellocq, using a Bellocq cannula or a soft-rubber catheter and tampon attached to a string, which is secured to the cheek with adhesive plaster. The packing must be removed and, if necessary, renewed after 24 hours in order to prevent systemic infection. (3) Cauterize the bleeding area with 20 per cent silver nitrate or with the actual cautery.

Give the cause, symptoms and treatment of immersion foot.

It is due to changes in the blood vessels resulting from long exposure to cold, without actual freezing of tissues. The symptoms are redness and swelling of the part with increasing impairment of circulation. The damage may be superficial with or without blisters, or deep with gangrene of the skin and subcutaneous tissues.

Treatment is prophylactic. The patient is treated systemically. Specific therapy consists of keeping the patient in a cold room and allowing the part to warm up gradually without overheating. Then the extremity is covered with a sterile cotton dressing. Local circulation is encouraged by vasodilating drugs, sympathetic nerve blocks and peripheral nerve blocks, passive motion, heat to other parts of the body, and anticoagulants to prevent progressive thrombosis. Infection and even gangrene may occur and are treated as indicated.

Describe the symptoms and give the treatment of hemorrhage from the middle meningeal artery.

Symptoms: The first symptoms are those of concussion. These are followed by a temporary return of consciousness and the gradual onset of *coma,* usually within twenty-four hours, often without any rise in the temperature. Slowly progressive paralysis secondary to pressure over the motor cortex is commonly seen and may be accompanied by twitching or jacksonian convulsions. The paralysis may begin in the face on the same side and then extend to the arm and leg on the side opposite to the injury. The pupil on the same side may be dilated and immobile. Bradycardia, increase in systolic blood pressure, and slow stertorous or Cheyne-Stokes respirations are among the varied signs when the patient lapses into a second period of unconsciousness.

Treatment: After subtemporal decompression with exposure of the artery, the clot is washed away by gentle irrigation and the bleeding point secured by a transfixion ligature or silver clips. The area is then touched with a cautery, or hemostatic agents, such as fibrin foam, oxidized cellulose, gelatin sponge with or without thrombin, or muscle may be applied. Drainage of the wound may be optional.

Differentiate between true and false sacculated aneurysm.

The sac of a true sacculated aneurysm contains all the layers of the artery. In a false sacculated aneurysm one or more of the layers of the artery are absent.

Describe a dissecting aneurysm.

A dissecting aneurysm is one in which the blood ruptures through the intima and forces its way between the layers of the artery; the sac of the aneurysm is formed within the wall of the vessel.

What are the varieties of arteriovenous aneurysm? State the points of difference.

An arteriovenous aneurysm is either an aneurysmal varix or a varicose aneurysm. An *aneurysmal varix* is a direct communication between an artery and a vein, without the interposition of a sac. A *varicose aneurysm* is an indirect communication between an artery and a vein with the interposition of a sac.

Describe the treatment for aortic aneurysm.

Saccular aneurysms which arise high in the ascending aorta or at the arch can be treated by mobilizing the neck of the aneurysm, cross clamping and excision of the sac, with suturing of the arterial wall at the neck. Aneurysms of the descending aorta are best treated by excision and grafting with fresh, deep-frozen, or freeze-dried homografts or synthetic cloth mesh prostheses used to bridge the defect. Certain aneurysms arising in the ascending aorta, fusiform aneurysms of the ascending aorta or arch, and aneurysms involving the celiac axis or renal arteries cannot be treated by these methods.

What surgical procedures are commonly used in the treatment of varicose veins of the lower extremity?

With adequate deep venous return the operative procedure is *ligation* of the long saphenous vein and its uppermost branches at the saphenofemoral junction. If there are incompetent valves of the communicating veins of the thigh as well as of the long saphenous vein, then, in addition to the above procedure, the incompetent communicating veins are ligated and excised. Ligation of the lesser saphenous vein in the popliteal space is performed for varicosities of the lesser saphenous system. Subcutaneous stripping of the veins is often necessary for more severe cases.

Treatment by *injection* of sclerosing solutions is employed for those varicosities that recur after ligation and excision, for small thin-walled varicose veins in young women, and for enlargement of cutaneous veins.

Give the symptoms and treatment of phlebitis of the deep veins of the lower extremity.

Symptoms: At first there is a pitting edema of the extremity, with a cyanotic color. This later develops into a hard, white edema. The skin temperature over the calf muscles may be elevated. Tenderness may be elicited over the lateral plantar surface of the foot and along the course of the posterior tibial vein, the popliteal vein, and the femoral vein. Homans' sign is positive, i.e., pain and muscle spasm in the calf when the foot is dorsiflexed.

Treatment: Bed rest with elevation of the foot of the bed. Mild heat may be applied by a light and cradle or by warm applications. An elastic bandage is applied from the toes to the groin. Anticoagulants in the form of parenteral heparin or oral Dicumarol should be given only under careful supervision and with the proper laboratory studies as a guide. Other similar anticoagulants are available.

Paravertebral lumbar sympathetic procaine (Novocain) blocks reduce the arterial and venous spasm present, thus allowing the limb to become warm, dry, and less edematous. X-ray therapy has been used to treat the periphlebitis. Division of the vein proximal to the clot may be performed in selected cases.

What are some of the etiologic factors in peripheral vascular disease?

Diabetes, long-standing chronic infections, improper diet, tobacco (particularly cigarettes), instability of sympathetic nervous system.

What are some of the methods of conservative treatment in peripheral vascular disease?

Correction of the etiological factor wherever possible; postural exercises; alternating suction and pressure by means of the "positive-negative" pressure boot; meticulous care of the feet; increase of blood volume and decrease of blood viscosity; reflex vasodilatation produced by immersing arms in warm water; interruption of sympathetic nerve function by procaine (Novocain) injection or appropriate surgical procedures; sympatholytic, adrenolytic, vasodilatory, or anticoagulant drugs.

What operative procedures are employed in the treatment of peripheral vascular disease?

Periarterial sympathectomy, sympathetic preganglion- and/or ganglionectomy, neurectomy, amputations, crushing selected peripheral nerves, arterial grafting.

What are the surgical procedures used in the treatment of hypertension?

Lumbar sympathectomy combined with splanchnicecotomy, celiac ganglionectomy and/or excision of varying amounts of thoracic sympathectomy chains are accepted procedures, as well as resection of coarctation of the aorta, or nephrectomy for unilateral kidney disease in specific patients. Total or subtotal adrenalectomy combined with adrenal denervation has been proposed for selected cases from success in preliminary trials. Pheochromocytoma of the adrenal gland can be removed with good results if proper anesthetic and postoperative management are administered. These tumors may be malignant.

INJURIES OF NERVES

What symptoms follow division of the facial nerve outside the skull?

Paralysis of the same side of the face without involvement of the palate or uvula. The paralyzed side of the face is immobile, devoid of expression, and the natural folds and wrinkles are obscured.

The eyelids cannot be completely closed, the eyeball rolling upward and outward when forcible closure is attempted. Epiphora is present because of the drooping of the lower lid. The lips cannot be firmly closed, and whistling is impossible. If attempts are made to move the face, marked asymmetry is produced, and the mouth is drawn toward the nonparalyzed side. Owing to the paralysis of the buccinator, food collects between the teeth and the cheek.

What are the signs and symptoms of total transection of the spinal cord following compression fracture?

There are complete paraplegia and flaccid paralysis distal to the level of the injury. Sensory loss is noted over the same area, with a zone of hyperesthesia at the level of the injury. Urinary and fecal retention, or fecal incontinence, priapism, and elevation of skin temperatures distal to the level of compression ensue. Compression injuries with incomplete transection can be benefited by early laminectomy.

Give the symptoms and treatment of section of the median nerve.

Symptoms: If the nerve is divided just above the wrist, there will be anesthesia over the radial side of the palm, over the palmar aspect of the thumb, index, middle, and half of the ring fingers, and over the dorsal aspect of the terminal phalanges of the same fingers. There will be paralysis of the outer group of the short muscles of the thumb and adduction will be impaired. The two lateral lumbricals will also be paralyzed causing loss of power of flexion of the index and middle fingers at the metacarpophalangeal articulation.

If the nerve is divided at the bend of the elbow or in the arm, there will be, in addition to the previously mentioned symptoms, a loss of pronation, loss of power in the hand grasp, particularly on the radial side, and probable hyperextension of the wrist.

Treatment: The wound should be enlarged, if necessary, and the ends of the nerve identified and sutured together with fine silk. The ends should be accurately approximated without tension. Massage and electrical stimulation should be given daily after the first week. The regeneration of the nerve can be expected at the rate of 1 mm. a day, or 1 inch a month.

What symptoms follow division of the radial nerve in the forearm?

Wrist drop and inability to extend the wrist or proximal phalanges and to adduct the thumb in the plane of the palm. There may or may not be anesthesia over the dorsal aspect of the radial side of the hand and thumb and the proximal phalanges of index and middle fingers.

What are the symptoms when the ulnar nerve has been divided on a level with the pisiform bone?

Paralysis of the muscles of the little finger, the inner half of the flexor brevis, and the adductor pollicis. It becomes impossible to adduct the thumb, and most movements of the little finger are abolished. Flexion of the ring and little fingers at the first joint is impossible. A condition known as *claw hand* is produced by the opponents of the interossei acting without normal opposition; it consists in overextension of the first phalanges and flexion of the others. The area of anesthesia in ulnar paralysis is the ulnar half of the hand, both front and back, the little finger and half of the ring finger, both front and back.

What symptoms follow injury of the common peroneal nerve?

Steppage gait is caused by foot drop, flexion of the toes and inversion of the foot after paralysis of the peronei, the long and short extensors of the toes and the tibialis anterior. Sensory loss is noted over the lateral half of the anterior surface of the leg and the dorsum of the foot to the proximal phalanges of the toes.

What operative procedures may be used in restoring function following loss of nerve substance?

Nerve implantation, nerve transference, nerve grafting, nerve stretching, change in position of adjacent joints, or a combination of these procedures may be used.

List the common causes for unsuccessful neurorrhaphy.

(1) Badly fibrosed distal stump; (2) proximal stump fibrosis; (3) poor anastomosis; (4) badly scarred bed; (5) disruption of the suture site.

DISEASES OF MUSCLES

What are the principal lesions of muscles?

Contusion, sprain, rupture of the sheath, rupture of muscle or tendon, congenital anomalies, laceration, myositis (traumatic, rheumatic, acute suppurative, tuberculous, syphilitic, parasitic, and myositis ossificans), atrophy, dystrophy, primary tumors (angioma, fibroma, chondroma, myxoma, and sarcoma), and secondary tumors.

What is the most common site of rupture of the quadriceps extensor femoris? Give the symptoms and treatment.

The site of the rupture is usually just above the insertion into the patella.

Symptoms: Pain just above the patella after sudden muscular exertion, with inability to extend the leg. On local examination, a defect is palpated about 1 cm. wide, extending across the thigh between the ruptured ends.

Treatment: Suture the tendon immediately and place the thigh and leg on a posterior splint. If operative treatment is impossible, strap the patella in place on a posterior splint. The leg should be extended on the thigh and the thigh flexed on the pelvis.

DISEASES OF JOINTS

How can ankylosis be prevented after injury to a joint?

Correct any alteration in the contour of the bearing surfaces, wrap with compression bandage, and immobilize the part until the acute reaction has subsided. After disappearance of the effusion, mild exercises and heat and massage may be employed, avoiding those activities that produce pain. When a weight-bearing joint is injured, proper shoes should be worn, and the joint should be protected by a splint, elastic bandage, or adhesive strapping.

Describe a surgical method for the reestablishment of joint function in confirmed ankylosis.

An arthroplasty is performed: Expose the joint, resect the bone ends, interpose autogenous fascia and plastic prostheses into the joint. Each case must be judged by its individual requirements. In instances in which stability and freedom from pain are more desirable than mobility, the joint can be fused in the optimum position by the operations of arthrodesis, erasion, or excision. In some instances in which arthroplasty is impossible, arthrodesis can be successfully performed.

How should ankylosis of the jaw be treated?

The treatment is determined by the cause and type of ankylosis. In the fibrous type, the jaws are gradually stretched by frequent application of an intermaxillary dilating apparatus. If the ankylosis is of long standing and the former method is unsuccessful, the condyles must be freed and a flap of deep fascia interposed within the joint. Transection of the rami of the mandible may be used in selected patients.

What are the principal pathologic conditions which involve the synovial bursae?

Acute simple traumatic bursitis, acute suppurative bursitis, chronic bursitis with effusion ("housemaid's knee"), chronic tuberculous bursitis, syphilitic and gouty deposits.

Define the following terms: (a) bursitis, (b) bunion, and (c) paronychia. Give the treatment for each disease.

(*a*) *Bursitis:* Inflammation of a bursa.

TREATMENT: Traumatic: aspiration and firm bandage; aspiration followed by injection of antiseptic solution, procaine (Novocain), and compound F. Infectious: drainage and antibiotics. Chronic: needling, excision, or x-ray therapy.

(*b*) *Bunion:* An enlargement of one of the bursae about the foot, usually on the inner side of the metatarsal joint of the great toe.

TREATMENT: Correctly made shoes and removal of pressure. If these fail, remove the inner end of the phalanx and the exuberant bone on the inner surface of the distal end of the first metatarsal bone.

(*c*) *Paronychia:* Pyogenic infection lateral to the nail beneath the eponychium.

TREATMENT: Adequate drainage. This varies, ranging from elevating the skin edge from the nail to excision of the proximal half of the nail with parallel lateral incisions through the eponychium and the latter reflected backward. In addition, elevation of the part, warm wet dressings, and proper antibiotics may be employed.

Where are swelling and fluctuation most prominent in synovitis of the ankle joint?

Between the external malleolus and the tendon of the communis digitorum and between the internal malleolus and the tendon of the tibialis anticus.

DISEASES OF BONES

Name the inflammatory diseases of bone.

Periostitis, osteitis, and osteomyelitis, or any combination of the three.

Give the etiology and treatment of osteomyelitis (periosteomyelitis). What part of the bone does it usually affect?

Acute osteomyelitis is usually due to *Staphylococcus aureus.* The streptococcus, colon bacillus, pneumococcus, and, very rarely, the gonococcus may also be the etiological microorganisms. Typhoid fever, tuberculosis, and syphilis are the most common causes of the *chronic* form. Osteomyelitis chiefly affects metaphyses of the long bones.

Treatment: ACUTE OSTEOMYELITIS: Massive doses of antibiotics, i.e., penicillin and/or streptomycin, or erythromycin. *Supportive treatment:* transfusions; immobilization, plus hot wet dressings. This treatment is often all that is required. Operative intervention may be necessary to provide drainage of an abscess close to the epiphyseal line on the side of the metaphysis. Pus is frequently found between the periosteum and the bone, and the medullary cavity is frequently involved. Small openings are made to drain the bone and the canal. The limb is immobilized and the dressings are not changed for one to several weeks.

CHRONIC OSTEOMYELITIS: Supportive treatment by blood transfusions and the appropriate antimicrobial therapy are important. Drainage is maintained until sequestration is complete, at which time the diseased bone is removed. A gutter the entire length of the involved shaft may be made, leaving the wound packed open with petrolatum gauze. In either case the limb is usually immobilized in plaster and redressed at infrequent intervals (Orr method or some modification of it).

Give the diagnosis and treatment of Pott's disease.

Diagnosis: The symptoms of Pott's disease are: Rigidity of the spine, detected by getting the patient to pick up an object from the floor or to rise from a dorsal recumbent posture. In consequence of the rigidity and tenderness, the gait is shuffling and uncertain. Pain and tenderness are elicited at times by jarring the head, by inducing the patient to jump from a chair or step, or by direct pressure. There is a constant tendency to support the back; the patient will frequently lie down and, when sitting up, will support the weight of the shoulders on the thighs. Reflex irritation is common. Lumbar disease is frequently attended with colicky pain, irritation of the bladder, and incontinence of urine. Cervical disease may cause torticollis or difficulty in deglutition. The deformity consists in an undue prominence of the spinous processes, causing a backward projection. Abscesses frequently develop. Paralysis is a late symptom.

Treatment: CONSTITUTIONAL: As for other tuberculous infections, including specific antimicrobial therapy (streptomycin, para-aminosalicylic acid, or isonicotinic acid in combination).

LOCAL: Bradford frame; extension of spine including the neck if cervical vertebrae are involved. This is maintained until all acute symptoms subside. After that, immobilization in plaster of paris or by a spinal brace. Direct fixation of the spine by autogenous bone graft is also employed.

ORTHOPEDICS

Dislocations

What is a dislocation (luxation)? Define the various kinds of dislocation.

The displacement of the articular surfaces of one or more bones of a joint from their normal relation to each other.

Classification in regard to cause: *traumatic,* due to either violence or muscular action; *pathological,* due to either alterations of the joint from disease or paralysis of the surrounding muscles; *congenital,* due to congenital malformation of the joint.

Classification as to degree: *complete,* an entire separation of the articular surfaces from each other; *partial,* the articular surfaces remaining in contact through a portion of their surface.

Classification as to time: *recent,* when sufficient time has not elapsed for inflammatory changes seriously to impede reduction; *old,* when such changes have taken place.

The terms "closed," "open," and "complicated" are applied to luxations precisely as in the case of fractures. The direction of the distal bone is often designated; i.e., superior, anterior, etc.

List the causes of dislocation. Give the cardinal symptoms of dislocation.

Predisposing causes: (1) the anatomical characteristics of the joint, (2) active adult life, (3) male sex, (4) disease. *Exciting causes:* (1) trauma (direct or indirect), (2) muscular action.

Symptoms: (1) an alteration in the shape of the joint, (2) an alteration in the length of the affected member (shortening or lengthening), (3) an alteration in the direction of the axis of the extremity, (4) the displaced articular surface is frequently felt in an abnormal position, (5) more or less immobility of the affected joint, (6) pain, swelling, and ecchymosis.

What articular changes take place in dislocation? What are the general principles governing the treatment of dislocation?

There is rupture or laceration of the ligaments and the capsule of the joint, and a change in the mutual relations of the articular ends of the bones. If the dislocation remains unreduced, the cavity of the joint becomes filled with granulation tissue and the displaced and lacerated tissues become thickened about the head of the dislocated bone. Any irregularities of the dislocated bone become rounded off, and the surrounding tissues form a false joint.

Principles of Treatment: Relaxation of muscles about the joint; reduction of the dislocation by causing the dislocated bone to enter the capsule through the same rent which it made upon leaving it (by manipulation, traction, and countertraction); fixation of the parts after reduction, followed by massage, and active and passive motion after about ten days.

List obstacles to reduction of dislocations.

Anatomical peculiarities of the joint, muscular resistance, the interposition of a portion of the capsular ligament or a muscle, fracture of the bone involved, and the presence of adhesions (old dislocations).

State the complications that may commonly occur during the reduction of a dislocation.

Fracture of the bone, rupture of the vessels, and injuries to the nerves.

Outline the principles of treatment of an open dislocation.

Cleanse and debride the wound. Reduce the dislocation and follow with proper immobilization. Give tetanus antitoxin, gas antiserum if indicated, and appropriate antibiotic therapy.

Describe a method of reduction of a dislocation of the mandible (inferior maxillary bone).

The patient is seated; the physician stands behind the patient and presses down upon the molar teeth with his two thumbs, which are guarded by a towel. This pressure is continued in a downward and backward direction until the condyle clears the eminentia articularis; then the chin is raised by the fingers, and the condyle snaps in place. The jaw should be immobilized for one week by a Barton bandage and the patient should not open his mouth widely for several months.

Describe the diagnosis and treatment of acromioclavicular dislocation.

There is a history of injury with swelling and pain over the tip of the shoulder and inability to use the arm and shoulder. The outer end of the clavicle is more prominent and movable when compared with that of the opposite side. In doubtful cases, the clinical diagnosis should be confirmed by x-ray examination of both shoulders.

Treatment: Reduction is accomplished by outward and backward traction on the shoulder, accompanied by downward pressure on the prominent end of the clavicle and the position maintained by an adhesive dressing. The outer end of the clavicle is padded as well as the elbow. A 2-inch wide adhesive bandage is applied from the midline of the back below the scapula upward and outward over the padded clavicle, down the arm to the elbow, curved beneath the elbow and up the opposite surface, crossing the clavicle again, and continuing across the front of the chest. The strapping requires retightening every few days, and healing is usually complete in 4 or 5 weeks. Surgical fixation may be necessary.

Name the varieties of shoulder-joint dislocation.

Subcoracoid, subglenoid, subclavicular, subspinous, superclavicular, and luxatio erecta.

What are the methods of reduction in subcoracoid dislocation of the humerus?

Reduction by manipulation (Kocher's, Cooper's methods). Extension and traction. Traction in an outward and upward direction. Some dislocations may be reduced by simply allowing the arm to hang over the side of a bed or table. By this method, reduction takes place through traction due to the weight of the arm. X-ray examination and general anesthesia are advised in most cases.

Describe any one of the dislocations of the shoulder joint and the mode of reduction.

Subcoracoid is the most common of the shoulder dislocations. In this dislocation the head of the humerus is felt in the axilla beneath the coracoid process. The shoulder is flattened, and the absence of the head beneath the acromion process is noted. The humerus stands out from the side and is somewhat oblique in direction, the elbow being carried back by the latissimus dorsi and teres major muscles. Voluntary movements are usually lost. Passively, the arm can be easily abducted but cannot be so far adducted as to bring the hand upon the opposite shoulder and the elbow to the front of the chest (Dugas' sign). Measurement from the acromion to the external condyle shows about ¾ inch shortening.

Reduction by Kocher's Manipulation: Flex the forearm on the arm to relax the long head of the biceps; raise the arm from the body to relax the deltoid and supraspinatus; rotate the humerus outward to relax the infraspinatus and teres minor; make forcible traction upon the humerus with one hand, sweep it to the side of the body and rotate it inward, carrying the forearm across the chest. This method may be facilitated by having an assistant place his hand in the axilla in order to manipulate the bone into place. However, reduction by traction and manipulation with the patient under general anesthesia is less apt to cause a fracture.

How would you diagnose and reduce a backward dislocation of the forearm?

In posterior dislocation of the elbow, the olecranon projects posteriorly; it is out of line with the condyles, and the distance between it and the condyles is greatly increased. The head of the radius is felt behind the external condyle as a smooth, broad, rounded projection; the articular extremity of the humerus can be felt in front of the elbow, below the joint crease. The forearm is flexed, supinated, and rigid. Measurements from the external condyle to the styloid process of the radius show shortening.

Treatment: If general anesthesia is contraindicated, a brachial block or local infiltration is used. Traction is made with the forearm in complete extension to slip the coronoid process of the ulna below the trochlea after any lateral subluxation has been reduced. After continued traction and manipulation a distinct snap indicates reduction. Immobilization is maintained for three weeks by an internal right angle splint or plaster splint. After that, physiotherapy and active use are indicated but not passive motion or stretching of the joint.

List the methods of reducing the dislocations of the terminal phalanx.

The methods employed are extension, traction and manipulation, and extreme extension.

List four varieties of hip joint dislocation and describe in detail two of these varieties.

(1) Upward and backward on dorsum ilii—*dorsal.* (2) Backward in sciatic notch—*ischiatic.* (3) Forward and downward in obturator foramen—*obturator.* (4) Forward and upon the pubis—*suprapubic.*

Dorsal Dislocation: In this variety the head of the bone rests upon the dorsum ilii, the trochanter is above Nélaton's line, the iliotibial band is relaxed, and there is shortening of 2 or 3 inches. If a patient is recumbent and the knees vertical, the foot of the injured extremity touches the bed, but the foot of the sound extremity is free of the bed (Allis' sign). A marked hollow is present in the upper part of Scarpa's triangle, and the head of the bone cannot be felt in its usual position. The thigh is flexed, adducted, and inverted, so that the axis of the femur crosses the lower third of the sound thigh, and the ball of the toe rests upon the opposite instep. The ligamentum teres is torn, and the capsule is lacerated. The small external rotator muscles are usually lacerated, but the iliofemoral ligament is usually uninjured.

Ischiatic Dislocation: The signs of this dislocation are somewhat similar, but less marked than in the preceding one. There is not so much shortening, for the intact obturator internus tendon prevents the head of the bone from traveling upward. The shortening is not more than ½ or 1 inch, but it becomes more apparent upon flexing the thigh. The thigh is flexed, adducted, and inverted; the axis of the femur crosses the opposite knee, and the great toe rests against the ball of the great toe of the sound side. Practically the same muscles and ligaments are injured as in the dorsal variety.

What are the complications of dislocation of the hip?

Fracture of the acetabulum, fracture of the femur, rupture of the femoral vessels, and injury to the blood supply to the femoral head, followed by necrosis, paralysis from compression or rupture of a nerve trunk, and extensive laceration of adjacent soft parts.

Describe a luxation of the hip joint and a method of reduction.

Dislocation downward into the obturator foramen: This dislocation is indicated by the following symptoms: the hip is flattened; the head of the bone is felt in its new position and is missed from the acetabulum; rigidity exists; passive motion is slight; a hollow is noted over the great trochanter. The trochanter is below Nélaton's line and nearer than normal to the middle line. The gluteal crease is lower on the injured side. There is lengthening to the extent of 1 to 2 inches. The body is bent forward by the traction upon the psoas and iliacus muscles. The limb is advanced and partially flexed and abducted. The foot is pointed straight ahead or is a little everted. When the patient is recumbent, extension is impossible, the knees cannot be pushed together without great pain, and the adductor muscles are hard and rigid. *Allis' sign* is absent. Reduce by manipulation if possible; if this fails, by extension.

To reduce by manipulation, flex the leg on the thigh and the thigh on the pelvis, and then perform, in the following order, abduction, internal circumduction, and extension.

List the dislocations of the ankle joint. Describe any one with mode of reduction.

There are five forms of dislocation: lateral, medial, forward, backward, and upward.

In dislocation backward the foot is shortened, the tibia and fibula project in front, the heel is prominent, and the relation between the malleoli and the tarsus is altered. The method of reducing a dislocation of the ankle joint is to flex the leg on the thigh and the thigh on the pelvis of the anesthetized patient and have an assistant make counterextension from the knee, while the surgeon makes extension from the foot and at the same time rocks the astragalus into place.

How are dislocations distinguished from fractures?

Dislocations are characterized by more or less immobility and absence of crepitus. The deformity does not usually recur after reduction. The end of the bone is felt in an abnormal position and rotates with the rest of the bone. Fractures are characterized by preternatural mobility and the presence of crepitus. X-ray examinations give confirming information and avoid the dangers of attempting to demonstrate crepitus.

Fractures

Name and describe the different varieties of fracture.

Closed (simple): There is no communication with external air. *Open* (compound): The fracture communicates with external air. *Complete:* The entire thickness of the bone is broken. *Incomplete:* The entire thickness of the bone is not broken. *Multiple:* The bone is fractured in more than one place and the lines of fracture do not communicate. *Single:* The bone is fractured in one place only. *Comminuted:* The bone is fractured into a number of fragments and the lines of fracture communicate with each other. *Fissured:* There is a linear split without displacement. *Stellate:* The lines of fracture radiate from a central point. *Depressed:* There is crushing and a portion of the skull is below the surface. *Avulsion* (sprain): A small fragment is torn from the bone. *Impacted:* One fragment is driven into the other. *Transverse, longitudinal, oblique, and spiral:* The terms indicate the direction of the line of fracture. *Intracapsular and extracapsular:* Fractures about joints are classed as intracapsular (within the capsular ligament) and extracapsular (without the capsular ligament). *Epiphyseal:* In young persons epiphyseal separation occurs and constitutes epiphyseal fracture. *Direct* or *indirect:* This indicates whether the fracture occurred at the point struck.

List the different kinds of displacement in fracture. In what directions does the line of fracture extend in the case of the long bones?

Varieties of Displacement: Transverse, longitudinal, angular, and rotary.

Directions of Line of Fracture: Transverse, longitudinal, oblique, spiral, V-shaped, Y-shaped, and T-shaped.

Define a fracture. Give the causes and symptoms of fractures.

A fracture is a break or interruption of the continuity of a bone or cartilage.

Predisposing causes: age, male sex, occupation, and diseased conditions of the bone. *Direct causes:* direct and indirect trauma and muscular action.

Symptoms: deformity, loss of function, preternatural mobility, crepitus, and local signs of trauma.

What fractures do not show abnormal mobility? Under what circumstances is crepitus absent?

(*a*) Impacted fractures, incomplete fractures, and fractures of the skull. (*b*) In impacted and incomplete fractures, and where there is a great separation or overriding of the fragments, or where portions of muscle, tendon, or periosteum are interposed between the fragments.

What are the possible mechanical obstructions in the reduction of fractures?

Muscular spasm, the interposition of muscle tendon or other soft tissue between the ends of the fragments, and impaction of the fragments.

State the causes of delayed union and give treatment.

The constitutional causes are age, syphilis, rickets, osteomalacia, and general debility. The local causes are devitalization of tissues at the time of injury, improper reduction, inadequate fixation, infection, and interposition of soft parts.

Treatment: Prolonged immobilization, adequate reduction, and eradication of infection, if present, are essential. *Operative* procedures, such as multiple drilling or exposure of fracture site for open reduction. Step cut operation or bone plating may be employed when more radical treatment is required. Removal of sequestra and an attempt both surgically and by chemotherapy are necessary to combat infection if present.

Calcium, vitamin D, parathyroid hormone, and other mineral and endocrine products are not indicated unless there is definite constitutional evidence of a deficiency.

What are the indications for trephining in fractures of the skull?

Depressed fractures, simple or compound; symptoms of subdural or extradural hemorrhage; continuing symptoms of cerebral compression not responding favorably to spinal drainage and dehydration are common indications.

In what portion of the base of the skull may fractures lead to the escape of cerebrospinal fluid?

Cerebrospinal fluid may escape through the nose or into the subconjunctival tissues in fracture of the anterior fossa involving the cribriform plate of the ethmoid; it may escape through the ear or eustachian tube in fractures of the middle or posterior fossa through the petrous portion of the temporal bone.

Give the symptoms and treatment of fracture at the base of the skull.

Fracture of the *anterior fossa* is frequently compound and associated with subconjunctival ecchymosis and epistaxis. In fracture of the *middle fossa* there is hemorrhage from the mouth and ear, sometimes with the escape of cerebrospinal fluid. The cranial nerves are frequently injured by the fracture, especially the seventh and eighth. In fracture of the *posterior fossa* there is usually respiratory derangement. The blood gradually accumulates beneath the deep fascia and produces discoloration in the line of the posterior auricular artery (*Battle's sign*). The cranial nerves are frequently injured in the fossa. Optic neuritis often appears after the first week. In fracture of the base the temperature is subnormal during shock, rises to 100° or 101°F., and gradually falls to about normal and remains normal or subnormal unless infection is present.

Treatment: Treat the patient for shock as indicated. Observe closely the patient's state of consciousness and perform a baseline neurological examination. Record the pulse, respiration, temperature, and blood pressure at hourly intervals during the first 24 hours. Unless contraindicated, a spinal puncture should be made and the pressure determined by a manometer. If the pressure is high, 50 cc. of 50 per cent sucrose should be given intravenously; this may be repeated in 6 hours if necessary. The intracranial pressure may also be reduced by the administration of magnesium sulfate, by bowel or by mouth, or by careful removal of spinal fluid. Antibiotics are given parenterally to prevent meningitis. If the markedly increased intracranial pressure does not respond to hypertonic therapy and the patient becomes comatose, a decompression operation is indicated.

What are the symptoms of fracture of the body of the vertebrae? Give in detail the usual treatment.

Symptoms: Great displacement is unusual, but there is pain (which is increased by motion), tenderness, ecchymosis, and, rarely, motor and sensory paralysis. Priapism, ileus, cystitis, and retention of urine may occur with injury to the spinal cord.

Treatment: When the fracture exists without any paralysis, hyperextension can be maintained by a plaster cast, applied early, in fractures of the thoracic or lumbar spine, while cervical fractures may require traction or open reduction. Fracture with paralysis is an indication for immediate laminectomy to relieve pressure on the spinal cord. Careful nursing care is required to prevent decubitis ulcers and urinary-tract or pulmonary infection.

Give symptoms and treatment of fracture of the nasal bones.

Symptoms: Pain, tenderness, deformity, epistaxis, crepitus, deflection of the septum, and, rarely, preternatural mobility or emphysema.

Treatment: Reduction, with or without an anesthetic, by introducing a padded dressing forceps into the nasal cavities. A light metal splint may be used over the nose. The air passage should be watched for ten days at which time fixation of the fragments should be firm. Any tendency to displacement should be corrected and internal splints may be required.

How and in what part of the mandible is fracture most likely to occur and what is the treatment?

The cause is usually direct violence, but indirect violence (lateral pressure) may fracture the body anteriorly. The most frequent site of fracture is near the mental foramen or the angle.

Treatment: Correct the deformity with

great care and bring the teeth into normal alignment. Place wires about the teeth and rubber bands between the upper and lower teeth. If the patient is without teeth, hold the lower jaw against the upper by means of a Barton bandage. The patient should receive liquid food and the mouth should be washed frequently with a peroxide mouth wash. Vomiting can cause serious complications; the rubber bands can be readily cut if vomiting occurs.

Give the treatment of fracture of the ribs.

The affected side should be firmly strapped with strips of adhesive tape so as to limit its range of motion. These strips (2 inches wide) should extend beyond the median line, both anteriorly and posteriorly, and are to be applied from below upward, each strip overlapping about one third of its predecessor. Each strip should be put on while the chest is in a state of forced expiration. If the patient has severe pulmonary disease, strapping is not advisable. If the fracture is open, treat it as other open fractures, unless the pleura has been opened.

State the most common site of fracture of the clavicle and describe a method of treatment.

The junction of the outer and middle thirds of the bone.

Treatment: With the patient sitting on a stool, an assistant stands behind him and, with his knee between the scapulae, draws the patient's shoulders forcibly upward and backward. The surgeon manipulates the fragments into position. Reduction is maintained by a well-fitted posterior figure-of-eight plaster splint. Active use of both arms is permitted and the cast is usually removed in 4 to 6 weeks.

Discuss briefly the treatment for fractures of the lower end of the humerus.

Displacement of fragments interferes with the blood and nerve supply and the function and appearance of the arm. Immediate reduction is imperative to diminish the swelling and pressure on blood vessels and lymphatics. Closed reduction and immobilization in acute flexion is indicated in simple *supracondylar* and *transcondylar* fractures without swelling, disintegration of the skin, or impaired circulation in the extremity. *Longitudinal fractures* of the trochlea or capitellum and simple epicondylar fractures may be treated in this manner. Continuous traction is indicated in Y, T, and comminuted fractures with separation, where there is considerable swelling, tendency to bleb formation, and impaired or threatened blood supply to the extremity.

When there is obliteration of radial pulse and swelling that prevents the normal venous return, operation is indicated to avoid a Volkmann's ischemic contracture. Operation is also employed for compound fractures, those irreducible by manipulation, and those with primary nerve injury.

What surgical landmarks of the elbow joint would aid you by their position in the differential diagnosis between a fracture of the upper end of the radius and a posterior dislocation of the ulna?

In patients with a fracture, the head of the radius does not rotate freely and the three bony points are in alignment; in dislocation, the opposite is true. The bony points are the two condyles of the humerus and the tip of the olecranon process of the ulna.

What is Colles' fracture? How would you treat it?

Colles' fracture is a transverse, or nearly transverse, fracture of the lower end of the radius, between the limits of ¼ inch and 1½ inches above the wrist joint. The lower fragment sometimes rests upon the dorsum of the upper fragment.

Treatment: Reduce the deformity by hyperextension to unlock the fragments and relax the dorsal periosteum; follow by longitudinal traction to separate the fragments, and forced flexion to give proper alignment. Apply a splint of wood or molded plaster, holding the hand in slight ulnar deviation. In some cases the more extreme position of palmar flexion, ulnar deviation, and pronation (Cotton-Lodor position) is helpful in maintaining reduction, but the wrist should be placed in dorsi-flexion within a week. Passive motion is begun upon the fingers in twenty-four hours, and upon the wrist after the first 2 weeks. The splint is removed in 4 weeks, and a bandage is worn for a week or more.

How would you treat a case of fracture through the symphysis of the pubis with a rupture of the urethra?

If possible, a catheter may be passed into the bladder through the site of rupture. If this cannot be done easily with assurance that the catheter has passed into the bladder, a suprapubic cystotomy should be performed in order to pass the catheter. The pelvis should be encircled with a canvas binder, and the patient placed upon a Bradford frame. General supportive care and antibiotics should be given.

Describe a method of treatment of fracture of the shaft of the femur at the middle third.

A Balkan frame is erected. The limb is placed in a Thomas splint and extension applied either by means of adhesive plaster or by skeletal traction through the condyles of the femur. The entire apparatus is placed in balanced suspension by attaching it to the Balkan frame. Frequent bedside x-ray examinations are made to determine progress. The treatment is maintained until union is solid.

Give the indications for operating in an open fracture of the thigh and describe the operation in detail.

All compound fractures must be considered as emergencies demanding immediate operation. Treat shock if present. Examine for other injuries. Obtain x-rays. Apply skeletal traction if necessary. Protect the wound by a sterile pad while the entire limb is scrubbed for 10 minutes with white soap and sterile cotton or cleaned with benzine, ether, or alcohol, and then painted with an antiseptic. The operator then changes his gown and gloves and drapes the wound. The wound is then irrigated from below upward with large volumes of warm, sterile, isotonic salt solution. The operator again changes his gloves. The walls of the wound from the skin downward are excised. Hemostasis is maintained constantly. All small, completely detached fragments of bone are removed. The fracture is reduced and immobilized. Severed tendons and nerves are repaired. The wound is left packed open with gauze and closed secondarily. Experienced surgeons occasionally close the wound primarily, but the selection of these cases requires experience and judgment. The fracture must be adequately immobilized with a plaster splint or skeletal traction or intermedullary pinning. General supportive treatment includes treatment of shock, tetanus antitoxin, gas-bacillus antiserum if the wound has been contaminated by street dirt or cultivated field soil, and adequate doses of antibiotics.

Describe the varieties and the treatment of fracture of the patella.

Varieties: Transverse, longitudinal, and stellate or comminuted.

Treatment: There are two methods: nonoperative and operative. In the *nonoperative* treatment, the leg is splinted in extension to hold the fragments in apposition by the use of a posterior splint or cylinder cast from the upper thigh to the ankle. In the *operative* treatment, an incision is made over the patella, with dissection down to the fracture and the removal of blood clots and fringes of the capsule of the joint. The torn ligaments and capsule are sutured. Some surgeons prefer to excise part or all of the patella. Postoperatively, the leg is elevated for four weeks, with massage after the first week. After 4 weeks a plaster cylinder should be applied for 3 weeks and the patient allowed to walk on crutches.

Describe Pott's fracture. Name the structures involved and outline the treatment.

Pott's fracture is a fracture of the lower fifth of the fibula, produced by eversion and abduction of the foot. If eversion is the main or only movement, the force is exerted through the internal lateral ligament and breaks the internal malleolus squarely off at its base; then it presses the external malleolus outward, rupturing the tibiofibular ligament and breaking the fibula close above the malleolus. Sometimes, instead of a pure rupture of the ligaments, there is avulsion of the portion of the tibia to which they are attached.

Treatment: Reduce the fracture at the earliest possible moment. Do not wait for swelling to subside. The quickest and best way to avoid swelling is immediate reduction and immobilization. After reduction, put the limb in a cast with the foot at a right angle to the leg, with slight inversion and the heel well forward. The plaster should extend to the mid-thigh. In 4 weeks the cast may be bisected and removed daily for gentle massage and passive motion. The cast should be removed entirely at the end of the sixth or eighth week. A bandage should be worn for 2 additional weeks.

Give the differential diagnosis between fracture of the neck of the humerus and dislocation of the shoulder joint.

FRACTURE	DISLOCATION
Fracture line demonstrated by x-ray.	Dislocation, with or without fracture, demonstrated by x-ray.
Elbow readily approximated to side.	Elbow cannot be approximated to side without causing great pain.
Elbow can be made to touch chest with hand of affected extremity upon the sound shoulder.	Elbow cannot be made to touch chest with hand of affected extremity upon sound shoulder (Dugas' sign).
Crepitus present.	No crepitus.
Preternatural mobility present.	No mobility.
Shape of shoulder joint unchanged.	Flattening of shoulder joint, the head of the bone being felt in an abnormal position.
Deformity may recur after reduction.	Deformity does not recur after reduction.
Shortening of the arm.	Elongation may be present, or the arm may be of normal length.

Differentiate dislocation of the head of the femur from fracture of its neck, and give essentials of treatment of each.

DORSAL DISLOCATION	INTRACAPSULAR FRACTURE
Inversion of the foot.	Eversion of the foot.
Immobility.	Preternatural mobility.
Head of femur not felt in its natural position.	Head of femur felt in its natural position.
The buttock of the affected side is unduly prominent, due to the presence of the head of the femur.	Flattening of the hip, with the great trochanter moving in an arc of smaller radius, and relaxation of the iliotibial band.
Crepitus is absent.	Crepitus may be elicited (unless impaction is present).
Immediate shortening of 2 or 3 inches.	Immediate shortening of ½ inch, consecutive 2 or 3 inches
Rarely occurs after 45, and more common in the male.	Much more common in advanced life and in the female.
Trauma usually considerable.	Trauma may be trivial.
Displacement demonstrated by x-ray.	Fraction demonstrated by x-ray.

Treatment of Dislocation: Reduction by flexion of the leg upon the thigh, flexion of the thigh upon the abdomen, external circumduction, and extension. When reduction has been accomplished, the knees should be bandaged together and the patient kept in bed for 2 weeks.

Treatment of Fracture: The patient is

anesthetized and the pelvis firmly fixed. Both thighs are widely abducted and traction made upon the injured limb until shortening is overcome. The foot is placed at right angles to the leg and rotated internally. Reduction is maintained by internal fixation, external fixation by a plaster cast, or a combination of both. Internal fixation is commonly effected by pins, nails, plates, and, rarely, bone grafts. When bone grafts are used, external fixation is also required.

Orthopedic Surgery

Describe an operation for wryneck (torticollis).

Open tenotomy of the sternal and clavicular heads of the sternocleidomastoid muscle by means of an incision parallel with the clavicle, starting from the suprasternal notch and extending outward for 2 inches, dividing the skin, fascia, and sternal and clavicular portion of the muscle. Control hemorrhage; suture the wound without drainage. Hold the head in an overcorrected position and apply a plaster cast for 5 or 6 weeks and follow with exercises and physiotherapy.

Describe tendon transplantation.

Tendon transplantation consists in the transference of the tendon of the distal extremity of the muscle from its normal point of leverage to another point, thereby removing strong antagonistic muscle action and/or substituting to some degree for the action of a diseased or atrophied muscle.

Describe an operation for the cure of webbed fingers.

Didot's Operation: A flap the length of the finger and half its width is taken from the dorsal surface of one finger and the palmar surface of the other. Each of these flaps is carefully applied to the denuded area upon the finger, to which it is attached and secured by sutures.

Describe the several varieties of clubfoot.

In *talipes equinus* the heel is drawn up and the patient walks upon his toes and the heads of the metatarsal bones. In *talipes calcaneus* the toes are raised from the ground and the patient walks upon his heel. In *talipes varus* the anterior half of the foot is adducted, the inner side of the foot is raised, and the patient walks upon the outer side. In *talipes valgus* the anterior half of the foot is abducted and everted, the patient resting on the inner side of the foot. Various combinations of these forms are designated as follows: talipes equinovarus, talipes equinovalgus, talipes calcaneovarus, and talipes calcaneovalgus.

Describe talipes equinus and give its treatment.

In talipes equinus the heel is drawn up so that the patient walks upon the metatarsophalangeal joints and the toes. The degree of deformity ranges from those cases in which there is simply a slight elevation of the heel to those in which the foot is almost vertical and the plantar muscles and fascia so contracted that the patient walks upon the metatarsal bones, the toes being in a position of overextension.

Treatment: The mild cases may be treated by manipulation and plaster bandages, but subcutaneous division of the tendo achillis is usually required. The foot is subsequently placed in its normal position and put in plaster of paris. The foot is kept in plaster for 3 months, and a mechanical support, rendering extension beyond a right angle impossible, must be worn for a year. In severe cases it may be necessary to divide the plantar fascia and elongate the tendo achillis. In the most obstinate cases some surgeons excise the astragalus or perform a cuneiform osteotomy. The earlier treatment can be started the better.

Describe in detail the condition known as talipes equinovarus.

In talipes equinovarus the heel is drawn up and the anterior half of the foot is adducted and drawn inward. The inner border of the sole is concave, and traversed by a sulcus corresponding to the position of the midtarsal joint. The outer border is convex. The sole of the foot is arched from secondary contraction of the plantar fascia and some of the plantar muscles, and its center may be marked by a longitudinal crease due to a folding over of the outer metatarsal bones. The patient walks upon the outer border of the foot. In acquired cases the extensor and peroneal muscles are paralyzed; the tibialis anticus, tibialis posticus, flexor longus digitorum, and the tendo achillis are secondarily shortened. This is the most common type of deformity (found in 75 per cent of all cases of clubfeet).

Give the treatment for talipes calcaneus.

Division of the flexor tendons. If the tendo achillis is attenuated, it should be shortened. In other cases the tendon of the peroneus longus may be grafted into the tendo achillis. In the paralytic variety some form of apparatus must always be worn.

Give the differential diagnosis of congenital talipes equinovarus and paralytic talipes equinovarus.

In congenital talipes equinovarus the condition exists from birth; it is usually bilateral, the circulation is good, there is little wasting of the muscles, the electric reactions are impaired slightly, if at all, the growth of the bones is unimpaired, and furrows are present in the sole. In the paralytic variety, the condition, which is not developed until the second or third year, is usually due to anterior poliomyelitis. It is usually unilateral, the circulation is feeble, the muscles show extreme wasting, electric reactions are almost entirely absent in the paralyzed muscles, the growth of the bones is considerably diminished, and there are no furrows in the sole.

What is genu valgum? State how genu valgum should be treated.

Genu valgum (knock knee) results from an unnatural growth of the internal condyle, causing the shaft of the femur to curve inward and the internal lateral ligament of the knee joint to stretch. The knees are close together and the feet widely separated. It may occur in one knee or in both knees.

Treatment: In cases of active rickets, dietary and hygienic treatment of the disease are necessary. In early stages, the patient is forbidden to walk, and corrective manual manipulation should be carried out several times daily. Braces are effective. When the patient is allowed to walk, elevation of the medial side of the shoe is important. In *severe cases* osteotomy is necessary—usually in the supracondylar region of the femur, but at times high in the tibia. In older cases, a small wedge of bone is sometimes removed.

Give the symptoms and treatment of hammer toe.

Hammer toe is an angular flexion of one or more of the toes (especially the little and second) at the first phalangeal articulation, the third phalanx being either in line with the second or flexed on it. The proximal phalanx is usually extended. Hammer toe is the result of contraction of the plantar fibers of the lateral ligaments of the joint. Relief is afforded in early cases by manipulation and splinting. In older cases resection of the proximal interphalangeal joint followed by splinting is necessary. Complete excision of the first phalanx is rarely necessary.

Amputations

What circumstances demand amputation of an extremity?

Rapidly ascending gangrene or gangrene after the line of demarcation has formed; primary malignant growths of bones or recurrent, as well as some primary, malignant growths of soft structures; deformity; tabetic joints; caries in the stump or painful stump (reamputation); and a crushing injury with extensive devitalization of tissue.

Describe a method of amputation of the thigh.

Flaps are made by incisions through the skin and a circular incision is made through the muscles (so-called "mixed method"). After all aseptic precautions have been observed, the surgeon takes his position at the side of the extremity to be amputated and makes a straight incision upon each side of the thigh. These incisions commence at the level at which the bone is to be divided; they are 1½ times as long as the diameter of the limb at their point of origin, and divide the skin and subcutaneous tissue. The lower ends of these incisions should be connected by an anterior transverse incision, and the corners of the flaps rounded off. The anterior flap, consisting of skin and subcutaneous fat, is now raised. The posterior flap is then dissected up. The muscles are divided by a circular sweep of the knife.

An assistant retracts the muscular tissue, a cuff of periosteum is raised, and the bone is sawed through as high up in the wound as possible. After the main vessels have been secured, the tourniquet should be loosened and all bleeding points caught and ligated. The large nerves are drawn out and divided with scissors at the highest possible level. Any projecting tendons are retrenched. Hemorrhage is controlled by ligation of the undivided vessels.

Describe a modified circular amputation of the leg.

Cut semilunar skin flaps, lay them back, and cut circularly to the bone at the edge of the turned-up flap. Another method of modified circular amputation consists in adding to the circular cut a vertical incision down the front of the leg. In sawing the bones of the leg, the fibula is divided at a higher level than the tibia, and the anterior edge of the tibia is rounded.

Describe a method of amputation of the last phalanx.

Make a dorsal incision over the interphalangeal joint, cut the lateral ligaments, disarticulate the last phalanx, and cut the palmar or plantar flap from within outward. It should extend to the end of the finger.

Describe disarticulation at a metacarpophalangeal joint.

The Racket Method: The incision upon the dorsum is begun just above the head of the metacarpal bone; it is carried down to beyond the base of the phalanx and involves the skin only. One incision sweeps around the finger at the level of the web, going through the skin; the finger is extended and the palmar cut is carried to the bone; each lateral incision is carried to the bone, while the finger is bent in the opposite direction; the flaps are dissected back to the joint, the finger is strongly extended, the joint is opened from the palmar side, and disarticulation is effected.

Describe disarticulation at the wrist joint.

A circular incision is made, 1½ inches below the styloid process of the radius, the tendons divided, and the disarticulation accomplished.

Describe Larrey's method of amputation at the shoulder joint.

The incision begins just below and in front of the acromion process and passes vertically downward for 4 inches. From the center of this incision an oval incision is carried around the arm. The anterior structures are divided close to the bone, and the posterior structures are cut next. To disarticulate, incise the capsule transversely upon the head of the bone; while the arm is rotated outward, divide the subscapularis and, while the arm is rotated inward, divide the supraspinatus, infraspinatus, and the teres minor muscles. Divide away any tissue holding the humerus to the body, stop all hemorrhage, and suture the skin wound vertically.

Excisions

What are the conditions which render excision of the lower jaw advisable?

Malignant tumors of the mandible or of the adjacent tissues involving the bone secondarily are indications.

How is resection of the elbow joint performed?

The forearm is flexed and held across the chest of the patient by an assistant. A vertical incision 5 inches in length is made along the back of the joint, the center of the incision being to the inner side of the tip of the olecranon. The tendon of the triceps is now divided close to the olecranon. The tissues are separated from the lower end of the humerus and the upper end of the ulna, care being taken not to injure the ulnar nerve or the insertion of the biceps and brachialis anticus. The ulna and radius are divided just below their articular surfaces; the lower end of the humerus is next resected. All diseased synovial membrane and granulation tissue must be dissected away, all bleeding points caught and ligated. The divided end of the triceps and the fascia are sutured in place. The wound is closed with or without drainage, as the case requires.

What are the indications for excision of the knee joint?

Tuberculous disease, disorganization of the joint after pyemia or osteoarthritis, old neglected cases of poliomyelitis where there is a flail limb, and deformity due to bony ankylosis in a bad position.

Describe resection of the knee joint.

A semilunar incision is made extending from either side of the joint to a point 1 inch below the tuberosity of the tibia. Dissect up this flap; divide the patellar tendon and the lateral ligaments. Take out the patella and divide the crucial ligaments; saw off the lower end of the femur at right angles to the shaft, from behind forward. Saw the upper end of the tibia from behind forward. Remove all diseased tissue. Suture the patellar tendon and the lateral ligaments in place. Suture the skin edges together, with or without drainage. Apply a plaster cast from the toes to the midthigh.

In what type of case should arthroplasty be attempted?

In ankylosis of the hips, knees, or elbows in strong, vigorous patients between the ages of 20 and 40. It is contraindicated in ankylosis after destruction of the joint by tuberculosis. Cases most favorable for arthroplasty are those resulting from acute pyogenic infection associated with traumatic injuries. Preferably, the infection must have been quiescent for a year or more.

BURNS

Give a classification of burns.

First, second, and third degree, according to the depth of necrosis. A *first degree* burn is superficial and no blebs form, but there is edema and dilatation of the capillaries, and peeling usually follows. There is no scarring. *Second degree* burns are those with necrosis of the entire epidermis and varying depths of the dermis. Blisters form. These burns epithelialize from the gland crypts and hair follicles near the surface; rapidity varies according to the number of glands and follicles remaining. The amount of scarring also depends on this factor. *Third* degree or full thickness burns are those in which all of the epithelial elements are destroyed. The tissue is either charred or coagulated and has no circulation.

How can you estimate the percentage of the body surface which has been burned?

A rough estimate can be made as follows: The anterior surface of the trunk, the posterior surface of the trunk, each leg, and both arms represent 18 per cent of the body surface respectively, and the head is approximately 9 per cent. (Note that these values are multiples of 9.)

Both legs	36%
Both arms	18%
All of trunk	36%
Head	9%
Neck	1%
	100%

Give the treatment of severe burn shock.

Large quantities of fluids (colloidal substance and electrolytes) are necessary. Treatment must be individualized, but the amount of fluid necessary can be estimated by several methods. Evan's formula is one method widely used. The amount of colloid required for the first 24 hours is determined by estimating the second and third degree burned area in percentage of body surface. This percentage is multiplied by the weight of the patient in kilograms (1 kg. = 2.2 lb.) and this amount of fluid is given as colloidal substance, of which at least one half should be whole blood. An amount equal to the amount of colloidal substance is given as isotonic salt solution, in addition to 2,000 cc. of 5 per cent glucose in water (smaller amounts in children, patients with respiratory-tract burns, and older adults). One half of the total 24-hour requirement of fluids should be given the first 8 hours (i.e., 70 kg. [155 lb.] man with 40 per cent second and third degree burn: 70 × 40 = 2800).

Give 1,500 cc. blood in 24 hours
1,300 cc. plasma or dextrose, etc.
2,800 cc. P.S.S.
2,000 cc. 5 per cent glucose in water } i.v. or p.o.

Total 7,600 cc., 3,800 cc. to be given in 8 hours

Ample oxygen, morphine, and/or barbiturates in sparing amounts are used when indicated, and fluid therapy is further guided by careful hourly measurement of the urinary output.

What is the treatment of the burn wound?

Grossly contaminated areas are cleansed by irrigation with saline. Open and closed methods can be used for treatment. The open method is satisfactory for the perineum and face, whereas the closed method of petrolatum gauze with firm, not tight, pressure dressings is superior for the hands, feet, joint surfaces, entire trunk burns where neither the back nor front are free of burned areas, and granulating surfaces. Early surgical debridement and skin grafting are desirable, as soon as the general condition of the patient will permit and as soon as the depth of the tissue injury can be judged. Tetanus antitoxin or toxoid, antibiotic therapy, and maintenance of adequate nutrition are necessary adjuncts to good treatment. Fractures complicating burns should be adequately immobilized without external plaster casts.

NUCLEAR RADIATION INJURIES

Classify radiation injuries.

(1) *Whole-body Radiation Injury:* This is due to exposure to large amounts of penetrating gamma and/or neutron radiation at the time of the explosion of a nuclear weapon.

(2) *Surface Radiation Injury:* This is due principally to exposure to beta rays from contact or near contact, with radioactive material, such as fission products and induced radioactivity.

(3) *Internal Radiation Injury:* This results from the selective deposition, such as in bone or thyroid gland, of radioactive material inhaled or absorbed through the gastrointestinal tract or wounds.

Give the treatment for whole-body radiation injury.

At present there are no specific agents of proved value either for prophylaxis or for treatment after exposure to nuclear radiation. Therapy should be directed at restoration of water and electrolyte balance, maintenance of general nutrition, control of infection, and treatment for hemorrhage and anemia.

HEAD, NECK, AND CHEST

What diseases attack the antrum maxillae (Highmore)?

Hydrops, empyema, tuberculosis, benign tumors (chondroma, fibroma, osteoma), and malignant tumors (sarcoma and carcinoma).

What is harelip?

A congenital deformity of the upper lip due to nonfusion of the frontonasal process with the maxillary process. It is characterized by defect of a V-shaped portion of the upper lip, situated on either side of the middle line or on both sides.

Describe the operation for the correction of harelip and state the best time for its performance.

The choice of operation depends upon the size and variety of the cleft. In a simple case the edges should be neatly trimmed and united with sutures. An adhesive plaster dressing is applied to relieve tension on the sutures. If this is inadequate to the extent of the defect, there are several methods by which a flap may be split and the edges united, giving a better cosmetic result.

In cases of harelip without cleft palate the operation should be performed during the first few days of life; when the deformity is associated with cleft palate, the lip should be repaired first, and the palate later, usually between 1 to 3 years of age.

Give a description of cleft palate.

In *simple* cleft palate there is a V-shaped defect extending from the posterior portion of the mouth to the nasal cavities. In *complete* cleft palate, which may be *single* or *double,* the defect extends from the mouth through the alveolar margin of the maxilla into the nose.

Describe an operation for the correction of cleft palate.

The child is anesthetized through an endotracheal tube and placed in the horizontal position, with the head lower than the chest. The maxillary processes are approximated with Brophy's plates or Hammond's clamps. After the edges of the cleft have been pared, the periosteum and the mucous membrane of the mouth are elevated from the processes and sutured together. In order to approximate the edges it may be necessary to make lateral slits along the alveolar margin. The flaps may be supported with a tape. If the operation is delayed until the age of 4 or 5 years, it may be necessary to make flaps. Other operations employ a mucoperiosteal flap (Lane); relaxing incisions through the mucoperiosteum lateral to the cleft (Davis); or the "push-back" principle, in which the cleft is covered posteriorly by a flap of muscle, the anterior portion being closed by a simple plastic operation (Dorrance). The most successful operative results are obtained during the first weeks of life.

What glandular structures are most commonly affected in carcinoma of the anterior portion of the tongue?

The submental and submaxillary lymph nodes, the superficial cervical chain and the deep cervical chain, which includes the node of the tongue opposite the bifurcation of the carotid artery; and the deep cervical lymph nodes; the sublingual and submaxillary salivary glands may also be involved.

How would you treat carcinoma of the anterior portion of the tongue with no palpable lymph node enlargement?

Excise the lesion with an ipsilateral radical neck dissection and a contralateral superomohyoid neck dissection. The local lesion could be treated by irradiation instead of surgical excision, provided the mandible is not involved. If the mandible is involved, it would be excised at the time of the neck dissection.

What is the treatment of diphtheric stenosis of the larynx?

Tracheotomy should be performed immediately. The principal objective in the treatment of diphtheria is the neutralization of circulating antibody, which is most quickly accomplished with antitoxin. Antimicrobial therapy may be used in conjunction with antitoxin but is no substitute for it.

Give the clinical picture of benign mixed tumors occurring in the salivary glands.

A painless mass that appears in a salivary gland and slowly increases in size but is unrelated to salivary stimulation. A solid mass can be felt in the gland, not attached to the skin. Facial-nerve function remains unimpaired. Although the tumors are benign, their local recurrence rate is high and therefore they should be surgically excised.

What is the treatment of acute pyogenic parotitis?

Establish the patency of Stensen's duct. Administer antibiotics in large doses. If suppuration is detected, immediate incision and drainage is indicated.

What are the indications for thyroidectomy?

Solitary nodules, rapidly enlarging gland, toxic nodular goiters, malignancy, chronic thyroiditis, and selected cases of heart disease if radioactive iodine is not available.

Give a general description of the operation for subtotal thyroidectomy.

A transverse collar incision is made through the skin, and the depressor muscles of the thyroid cartilage are separated or divided. The isthmus is clamped, divided, and ligated. The superior thyroid vessels are doubly ligated; then the inferior thyroid vessels and the lobe are removed by resection of four sixths to five sixths of its total. A similar procedure is carried out on the other side. Care must be exercised not to go below the posterior sheath for fear of removing the parathyroids, or to excise the inferior medial portion of the gland without visualizing the recurrent laryngeal nerve. The wound is closed by separate suture of the stumps of the gland, the deep cervical fascia, the platysma, and the skin. Drainage is provided by a strip of rubber dam placed in each fossa. This is removed in 24 hours.

What is the treatment of branchiogenic cysts (bilateral cervical cysts or embryonic thymic cysts)?

Surgical excision under general anesthesia is the treatment of choice. Extension of the cyst to the pharyngeal mucosa is not uncommon and proper precautions are necessary to prevent pharyngeal cutaneous fistulae.

Where are the common sites for cysts of the thyroglossal duct?

The cysts may occur anywhere in the midline from the foramen cecum of the tongue to the pyramidal lobe of the thyroid gland. Extension above and below the hyoid bone is commonly found.

What is the incidence of carcinoma of the thyroid in patients with solitary nodules of the thyroid gland?

Several authors have reported series with an incidence of 15 to 25 per cent.

Chest

Give the symptoms and treatment of stricture of the esophagus.

The chief symptom is difficulty in swallowing. The dysphagia is first noted with dry solids, and finally with liquids. In some cases regurgitation occurs after swallowing. If the stricture is high, the regurgitation is almost immediate; if lower, it is delayed, especially if the canal is dilated above the stricture. The patient feels weak and hungry, becomes exhausted and emaciated, and suffers from flatulence and constipation. The stricture may be located by esophagoscopy and confirmed by x-ray examination of the swallowing function.

Treatment: Gradual dilatation through the mouth, if possible. If the stricture is situated above the sternum, esophagotomy should be considered. If below the sternum, perform a gastrostomy and retrograde dilatation. Pass a filiform bougie with a silk thread attached to it; with this silk thread, using a sawing movement, perform internal esophagotomy. If nothing can be passed, perform a jejunostomy preliminary to a resection of the stenosis and primary esophagogastrostomy, or replacement of the esophagus by the jejunum. If due to neoplasm, reset the lesion and restore the continuity between the esophagus and stomach.

Give the treatment for lung abscess.

If the lung abscess does not respond to medical treatment, most surgeons prefer to excise the lesion rather than drain it, since the incidence of residual bronchiectasis after drainage of lung abscess is high.

What measures should be carried out prior to performing any operation for empyema?

Aspirate and take a culture of the pus and examine the chest by x-ray when possible. In large or total effusions the collection should be evacuated by repeated aspirations, followed by intrapleural injections of antibiotics and/or lytic enzymes.

Describe the operation for empyema.

Acute Empyema: In the case of a child, perform thoracotomy and effect drainage by means of a large rubber tube placed in the most dependent portion of the cavity. In adults, rib resection is necessary. Suction should be applied to the tube; the chest wall is sealed about the tube by a rubber dam dressing glued to the skin and about the tube in an air-tight manner.

Chronic Empyema: The treatment is similar to that of acute empyema with strong suction applied to the intrathoracic drainage tube. Some cavities will then close, but others require thoracotomy and decortication, or a Schede type of thoracoplasty.

What is tension pneumothorax?

This condition is produced by a penetrating wound of the chest, in which the lung is injured by a fractured rib or a foreign body. As air escapes into the pleural cavity and is trapped, the pressure within the pleural cavity gradually increases, thus collapsing not only the lung on the side of injury, but, to somewhat lesser extent, the lung of the opposite side.

What condition prevents the successful induction of an artificial pneumothorax?

Adhesions between the lung and pleura which prevent collapse.

What is the surgical treatment of bronchiectasis?

Lobectomy, segmental resection of the affected lobe, or pneumonectomy.

What clinical findings usually suggest inoperability for carcinoma of the lung?

Distant metastases, bloody pleural effusion, recurrent laryngeal-nerve paralysis, phrenic-nerve paralysis with lesions in the upper thorax, extensive invasion of the trachea at or above the carina, severe cardiopulmonary insufficiency.

List the cardiac and great vessel lesions which are definitely aided by surgery.

Patent ductus arteriosus, coarctation of the aorta, double aortic arch, anomalous right subclavian artery, tetralogy of Fallot, valvular pulmonary stenosis, mitral stenosis, interauricular septal defect, aortic aneurysm, tricuspid atresia, lacerations, foreign bodies, acute and constrictive pericarditis, tumors of the heart. Other lesions in which surgery is of new or of unproved value: transposition of the great vessels, aortic stenosis, mitral and aortic insufficiency, interventricular septal defect, and coronary artery disease.

Discuss the surgical treatment of aortic stenosis.

Both open- and closed-heart techniques have been used. The valve can be dilated by a "blind" approach either through a transventricular route or retrograde through the ascending aorta. The "blind" techniques are still widely used, especially in correcting aortic stenosis present in combination with mitral stenosis; the mortality in this group has been approximately 10 per cent. However, in patients with isolated aortic stenosis, the surgical mortality has been at least 20 per cent. The reason for this difference in mortality between the two groups seems to stem from the fact that high grade mitral stenosis apparently "protects" the left ventricle from excessive hypertrophy. In contrast, in isolated aortic stenosis the left ventricle is greatly thickened and thus (1) seems more likely to fibrillate during surgery, (2) is more difficult to "pump" manually in maintaining circulation during ventricular fibrillation, and (3) is more difficult to defibrillate electrically. Thus, with the advent of methods for cardiopulmonary bypass, direct-vision surgery has been adopted in an effort to avoid these hazards of the "blind" approach in patients with isolated aortic stenosis.

ABDOMINAL SURGERY

What are the indications for the operation of gastrostomy?

Unresectable malignant disease of the esophagus; stricture or stenosis of the esophagus from any cause, when the patient is unable to take sufficient nourishment; at times, for retrograde dilatation of the esophagus. Sometimes established temporarily to facilitate treatment of stricture of the larynx.

Describe the posterior method of gastroenterostomy.

An incision about 5 inches long is made in the line of the right rectus from 1 inch below the margin of the ribs downward. The rectus muscle is divided in the line of its fibers and the posterior sheath in the same line. The peritoneum is divided between forceps. The most dependent portion of the stomach is located and grasped in forceps; the omentum and transverse colon are raised up and folded in a damp pad on the anterior abdominal surface; the ligament of Treitz and the beginning of the jejunum are located. Then the posterior layer of the transverse mesocolon is divided, and the most dependent portion of the stomach drawn through. The serous coats of the stomach and bowel are sutured together with interrupted silk sutures; then the stomach and intestine are opened. The edges of the stomach and intestinal wounds are sutured together with atraumatic chromic catgut, and the first layer or serous suture is continued with atraumatic chromic catgut to the original sutures. The defect in the mesentery is closed about the stomach, and the abdominal wound is closed.

What surgical procedures can be done for the treatment of carcinoma of the stomach?

Subtotal gastric resection with removal of omentum and wide excision of adjacent areas of lymphatic drainage;

total gastrectomy; esophagogastrectomy. Palliation can be offered to some patients by gastroenterostomy; rarely jejunostomy.

Give the symptoms and treatment of ruptured gastric ulcer.

Symptoms: Sudden and severe epigastric pain and profound collapse occurs. There is marked boardlike rigidity and tenderness in the upper abdomen. Liver dullness is greatly diminished. Vomiting of watery material sometimes occurs. X-ray of the abdomen in the upright position will show air beneath the right leaf of the diaphragm. The pain remains severe and constant, and may extend to the right lower quadrant.

Treatment: Immediate abdominal section with repair of the perforation and general supportive therapy and antibiotics. Subtotal gastric resection is occasionally performed under these circumstances.

What are the indications for surgery in duodenal ulcer?

Obstruction, hemorrhage, intractability to medical care, perforation. Malignancy and common bile duct obstruction are rarer complications.

Give the etiology of subphrenic abscess.

Subphrenic abscess is usually a sequel to abdominal surgery and to suppurative and perforative intra-abdominal lesions —appendicitis, perforated peptic ulcer, suppurative disease of the biliary tract, and pancreatitis. Only 10 per cent of cases arise outside of the abdomen.

Give the symptoms of gallstones in the common duct.

Irregular fever, frequently nausea and vomiting, and usually constipation. Jaundice is almost always present and varies in intensity from day to day. Pain may radiate to the back, and tenderness is present over Mayo-Robson's point. When the stone is passing down the duct, or when it passes into the duodenum, paroxysms of acute pain occur.

Give the treatment of stones in the common duct.

Perform an abdominal section and remove the stones by making an opening in the common duct. Insert a T-tube in the duct for drainage. Operative cholangiography should be employed. Supportive therapy consists of vitamins, crude liver extract, cholagogues, and antibiotics. High carbohydrate and high protein diet should be used, especially if severe hepatocellular damage is present secondary to common duct obstruction.

Describe the operation of cholecystectomy.

The peritoneum is opened through a right upper abdominal incision. The abdomen is explored; the head of the pancreas is carefully palpated as well as the extrahepatic biliary system. The intestines are packed away, and the gallbladder grasped with curved hemostats and drawn upward. If distended, the gallbladder may be isolated by sponges and aspirated. The common bile duct, cystic duct, and hepatic ducts are identified. The cystic duct is isolated and doubly ligated as is the cystic artery. The gallbladder is removed subperitoneally from below. A rubber drain is inserted along the cystic fossa to Morison's pouch, and a cigarette drain is placed in the foramen of Winslow. The drain is brought out through the incision or a lateral stab wound. The incision is closed in layers.

What are the symptoms and signs of acute hemorrhagic pancreatitis? Outline the treatment.

Severe epigastric pain and rigidity of sudden onset, usually accompanied by nausea, vomiting, ileus and abdominal distention, preclinical shock, jaundice of a varying degree, fever, frank edema, periumbilical discoloration; later a left hypogastric mass is often palpable. The serum and urinary amylase is elevated early and is diagnostic. The serum lipase remains elevated for a longer period. Hypocalcemia or hyperglycemia may occur secondarily and the leukocytic response is nonspecific.

Treatment: (1) Pain relief by anodynes and celiac block with procaine. (2) Intubation of the stomach, to relieve and prevent abdominal distention and to decrease the flow of acid over the duodenal mucosa and secondary pancreatic stimulation. (3) Atropine to decrease pancreatic secretion. (4) Antibiotics to control infection. (5) General supportive measures, blood, electrolytes and fluids, and calcium and insulin as necessary. (6) The formation of a cystic abscess and the presence of gallstones require surgical treatment. (7) If the diagnosis of pancreatitis has been made at operation, the biliary tract should be drained and the pancreas disturbed as little as possible. When portions of the pancreas have become necrotic in the later stages of the disease, these portions should be removed and drained.

Describe McBurney's gridiron incision for appendicitis. What is the advantage of this incision and what is the disadvantage?

An oblique incision about 4 inches in length, commencing 1 inch above McBurney's line and crossing this line about 1½ inches inside the anterior superior spine. The position of the incision will naturally vary somewhat, but it should always be made in the direction of the fibers of the external oblique muscle. The aponeurosis of the external oblique and a small portion of the muscle itself are now divided in the direction of the external incision. The fibers of the external oblique should be separated, great care being taken that none of the fibers are divided transversely. Retractors are now placed in the wound, and the internal oblique and transversalis muscles are similarly split in the direction of their fibers. The transversalis fascia and peritoneum are then divided in the usual manner.

The advantage of the incision is that the abdominal wall is not weakened as much as if the muscle fibers were cut across, and there is less tendency to subsequent ventral hernia. The incision is over the area of the appendix allowing less chance of contaminating the peritoneal cavity, a minimum of trauma, and therefore fewer later complications. The disadvantage of this incision is that the amount of room to work in is somewhat lessened and thorough abdominal exploration is consequently rendered more difficult.

What are the causes of intestinal obstruction?

Mechanical obstruction due to narrowed intestinal lumen resulting from strictures, congenital or acquired. The congenital variety is due either to atresia or to an imperforate membrane. The acquired variety is the result of inflammation, trauma, or a vascular or neoplastic lesion. Narrowing of the intestinal lumen may also result from obturation and compression from without by tumors or exudates. Obstruction often results from adhesions or bands that may be of congenital, inflammatory, traumatic, or neoplastic origin.

Other causes of mechanical obstruction are hernia, volvulus, intussusception, and developmental abnormalities. Vascular occlusion produces intestinal obstruction by mesenteric thrombosis and embolism. A form of obstruction results from nervous imbalance, such as paralytic ileus and spastic or dynamic obstruction.

Discuss the surgical treatment of Hirschsprung's disease.

It has been clearly shown that the true pathological process of this disease is located in the undilated portion of the rectosigmoid and not in the dilated and hypertrophied part of the large bowel. The treatment then is aimed toward removal of this abnormal and narrow area instead of procedures directly concerned with the dilated portion itself.

Define volvulus and give its treatment.

Volvulus, or the twisting of a loop of intestine around its axis, constitutes a well-defined form of intestinal obstruction. This pathological condition can occur only where the mesentery of the bowel is of sufficient length and is, therefore, most frequently met with in the lower portion of the ileum and at the sigmoid flexure of the colon. The immediate cause of the volvulus has been ascribed to the accumulation of intestinal contents above a constricted portion of bowel, and in a few cases to adhesions between an omental stump and an intestinal loop.

Treatment: Operate immediately after making the diagnosis. An attempt should be made to untwist the intestine. Since recurrence is frequent, the intestine should be fixed by means of plication, colopexy, or lateral anastomosis. Excision of the involved bowel is usually necessary either by the Mikulicz method or by primary anastomosis. If the patient is in poor condition and a large amount of large intestine is involved, perform a colostomy.

Enumerate the diagnostic points in intussusception.

Periodic attacks of colicky abdominal pain, vomiting, tenesmus, the passage of blood-stained mucus or pure blood, and the presence of a sausage-shaped tumor, which usually is situated in the line of the colon. In advanced cases rectal examination may reveal the presence of the intussusceptum. Acute intussusception is more common in early childhood; chronic intussusception is more frequently observed in adults.

What are the indications for splenectomy?

With the following conditions splenectomy is indicated: rupture, torsion, hypersplenism, neoplasms, cysts, hemangiomas, abscesses, schistosomiasis, aneurysms of the splenic artery, enlarged spleen with symptoms due to its size or position, and secondary involvement of the hilus of the spleen by a neoplasm of adjacent organs.

In the following conditions, splenectomy may be of value in selected patients: sickle-cell anemia, tuberculosis, Mediterranean anemia, Gaucher's disease, and portal hypertension.

Define "splenosis."

Spontaneous, traumatic, pathological or surgical rupture of the spleen may lead to a "seeding" of the peritoneal cavity and the subsequent development of "functioning" transplants, a condition known as "splenosis." The clinical recurrence of symptoms and signs suggestive of hypersplenism in a patient previously relieved of a similar syndrome by splenectomy should always be attributed, at least tentatively, to additional or accessory splenic tissue until proved otherwise.

(*a*) What surgical procedures are helpful in portal hypertension? (*b*) What are the indications and contraindications of portacaval shunt?

(*a*) Portacaval anastomosis and splenorenal anastomosis are the preferable procedures. Anastomosis of the superior mesenteric vein at the inferior vena cava, splenectomy, ligation of the hepatic artery, sclerosing agents injected into esophageal varices or multiple ligation of varices, or resection of the lower esophagus and upper stomach offer less hope for permanent correction.

(*b*) The indication for portacaval shunt is bleeding esophageal varices. Portacaval shunt should not be performed if the prothrombin time cannot be increased to near normal limits, if the bromsulfalein retention is greater than 35 per cent, if the plasma albumin is very low, if the serum bilirubin is more than slightly elevated, if there is marked increase in the liver flocculation tests, or if there is ascites that does not respond to medical treatment.

Describe the steps in the operation of a transverse colostomy.

An incision about 4 inches in length is made to the right and above the umbilicus and the transverse colon is delivered through the wound. The omentum is dissected free for several inches and a glass rod is placed under the bowel by perforating the mesocolon. The ends of the rod are connected to the ends of a rubber tube about 12 inches long. If more than one finger can be placed on each side of the bowel, the incision is partially closed. Petrolatum gauze dressings are applied about the bowel, supporting the glass rod. If immediate decompression is desirable, a rubber catheter can then be inserted into the bowel lumen through a purse-string suture placed in the anterior surface of the bowel.

How would you proceed surgically to remove the fluid in a case of ascites?

The patient should be propped up on an operating table, the bladder emptied by catheterization, and the lower abdomen sterilized. A point two thirds of the distance between the symphysis pubis and the umbilicus is anesthetized by a local method. A trocar and cannula, guarded by the thumb, should be inserted at that point. Almost all the fluid should be removed, the cannula withdrawn, and the puncture closed with gauze and collodion or a single silk suture. Lateral abdominal punctures can be made if necessary.

HERNIA

Describe the common anatomic varieties of abdominal hernia.

Indirect inguinal (*oblique, external inguinal*): The hernia enters the inguinal canal through the internal abdominal ring, lateral and superior to the deep epigastric artery. This variety is called "complete" if it passes through the external abdominal ring (scrotal hernia in the male, labial in the female); it is called "incomplete" (bubonocele) if it remains in the inguinal canal.

Direct or internal inguinal: The hernia gains entrance to the inguinal canal by passing through Hesselbach's triangle. It does not pass through the internal abdominal ring; the neck of the hernia is medial and inferior to the deep epigastric artery.

Femoral: The hernia passes out of the abdominal cavity through the femoral canal and makes its appearance upon the thigh through the saphenous opening.

Umbilical: The hernia passes through the umbilical ring.

Obturator: The hernia passes out of the abdominal cavity through the obturator canal and may make its appearance upon the inner surface of the thigh.

Sciatic: The hernia passes out of the pelvis through one of the sacrosciatic foramina, usually the greater, and makes its appearance at the lower border of the gluteus maximus.

Perineal: All hernias that protrude through the muscular floor of the pelvis toward the perineum are termed "perineal hernias."

Diaphragmatic: The hernia protrudes through the diaphragm.

Ventral: The hernia appears at any portion of the anterior abdominal wall except the umbilicus.

Lumbar: A hernia making its appearance in the lumbar region.

Internal: Hernia through the foramen of Winslow, through the duodenojejunal fossa, through the retrocecal or ileocecal recesses, or through the intersigmoid recess.

What are the predisposing and what are the exciting causes of abdominal hernia?

Predisposing Causes: Congenital defects, male sex, occupations demanding great muscular exertion, structural defects (elongation of the mesentery, patent funicular process), heredity, pertussis, bronchitis, urethral stricture, constipation, weakening of the abdominal wall by injury, operation, or pregnancy.

Exciting Cause: Any increase of the intra-abdominal pressure.

What is the cause of the impulse felt in a scrotal hernia on coughing? When is this impulse absent in such a hernia, and in what other condition resembling hernia may it be present?

In scrotal hernia the cavity is connected with the abdominal cavity, and any increase in the intra-abdominal pressure will, of course, be transmitted to the hernial sac. This impulse is absent when strangulation is present. An impulse may be present in a congenital hydrocele.

Describe (*a*) complete indirect inguinal hernia, (*b*) the symptoms of strangulation, (*c*) methods of reduction, and (*d*) operation if strangulation exists.

(*a*) In complete inguinal hernia the sac extends down into the scrotum in the male, into the labia majora in the female. It passes out through the internal abdominal ring into the inguinal canal, then through the external ring into the scrotum or labia.

(*b*) When strangulation begins, the patient is seized with pain about the hernial orifice and with violent colicky pain; the paroxysms of colic become more and more frequent, until finally the pain may be continuous. The hernia is irreducible, larger than usual, tender, painful, dull on percussion, does not transmit an impulse with coughing. Eructations of gas are frequent, and generally uncontrollable vomiting and prostration follow. Constipation is absolute, not even gas being passed. When gangrene begins, the symptoms lessen in severity.

(*c*) Grasp the hernia in the palm of the hand, and with the other hand assist the contents of the hernia that came out last to re-enter first, and so on until all of the hernia is reduced. In infants sedation with the buttocks placed higher than the head and shoulders will often allow spontaneous reduction of inguinal hernias.

(*d*) Perform the usual hernioplasty if the patient's condition will warrant it. If not, divide the constriction, examine the bowel, resect it if necessary, and close the wound with through and through sutures.

What tissues are divided in the operation for indirect inguinal hernia?

Skin, superficial and deep fascia, external and internal oblique muscles, and coverings of the sac (intercolumnar fascia, cremasteric fascia, infundibuliform fascia, subserous areolar tissue, and peritoneum).

Describe Bassini's operation for the treatment of an indirect inguinal hernia.

An incision is made parallel to and 1 inch above Poupart's ligament, extending from the external ring to a point on the abdominal wall opposite the internal ring. By this incision the aponeurosis of the external oblique and the external ring are exposed. Bleeding is controlled, the aponeurosis is incised in the direction of its fibers, from above downward, and the inguinal canal is opened. The aponeurosis of the external oblique is dissected until Poupart's ligament is exposed. A mass containing the sac of the hernia, the cord, the cremaster muscle, and fat is mobilized. Masses of fat, portions of spermatic veins, and usually the cremaster muscle are removed. The sac is isolated first at its neck, and the neck is stripped from the inner aspect of the internal ring for the distance of 1 inch. The sac is opened at the fundus, the interior is investigated, and, if the contents are reducible, they are reposited into the abdominal cavity, and the neck of the sac clamped. The neck of the sac above the clamp is tied off. High removal obviates leaving a funnel-shaped depression of peritoneum. The ends of the suture are then passed through the internal oblique muscle and tied, transfixing the sac. The cord is now lifted out of the way, the inner surface of Poupart's ligament is exposed by retraction, and the deep sutures are passed, uniting the conjoined tendon and the internal oblique muscle to the deep, shelving edge of Poupart's ligament. The sutures are tied from above downward. The cord is laid upon this new floor, and the aponeurosis of the external oblique is sutured over it. Interrupted sutures should be used.

What is incarceration of a hernia? How does it differ from strangulation?

The contents of the hernial sac become obstructed and irreducible, but the blood supply is maintained in incarceration while with strangulation the blood supply is arrested.

Describe an operation for the treatment of femoral hernia.

Either the inguinal or femoral approach may be used, but the high or inguinal operation is more convenient when strangulation is present. Also, suturing Poupart's ligament to Cooper's ligament closes the ring at its entrance. The incision is made as for an inguinal hernia except that it is continued down over the pubis. The inguinal canal is exposed and its floor in Hesselbach's triangle opened to expose the neck of the femoral sac. The sac is delivered from the femoral canal, opened, ligated and the distal portion excised. The femoral ring is closed from within by interrupted sutures. The transversalis fascia is repaired and the inguinal canal closed as in an inguinal hernia. Resection is performed if necessary.

Outline the treatment for irreducible umbilical hernia.

Gastrointestinal intubation and correction of the fluid and electrolyte balance. Early reduction and surgical repair, after careful examination of the contents of the sac and resection of the bowel if necessary.

Describe the operation for the treatment of an umbilical hernia.

Mayo's Operation: Transverse elliptic incisions are made around the umbilicus and hernia, and the neck of the sac is exposed. The surface of the aponeurosis is cleared for 1½ inches. The fibrous and peritoneal coverings of the hernia are divided by a circular incision around the neck of the sac. The intestines are freed from the adhesions and reposited within the abdomen. The omentum is ligated and removed with the sac. The margins of the ring are grasped and overlapped in order to indicate in which way it can be most easily done. An incision is made through the fibrous and peritoneal coverings of the ring, 1 inch or more transversely on each side, and the peritoneum is stripped from the under surface of the upper flap. Several mattress sutures are introduced 1 inch above the edge of the upper flap and carried through the margin of the lower flap; sufficient traction is made to permit closing of the peritoneum with a continuous catgut suture. When this has been accomplished, traction is placed upon the mattress sutures so as to slide the lower flap into the pocket between the peritoneum and the under surface of the upper flap. The free margin of the upper flap is fixed by catgut sutures to the aponeurosis, and the skin wound is closed in the usual manner.

TUMORS

What is a tumor?

A tumor is a pathological new growth that tends to persist independently of the structures in which it lies, and which performs no physiological function.

List the criteria for judging inoperability of carcinoma of the breast.

Patients are considered inoperable when the following conditions are present: (1) Extensive edema of the skin over the breast. (2) Satellite nodules in the skin over the breast. (3) Intercostal or paradermal nodules. (4) Edema of the arm. (5) Proved palpable supraclavicular nodes with metastases. (6) Inflammatory type of carcinoma. (7) Distant metastases. (8) When two or more of the following criteria are present: (*a*) ulceration of the skin, (*b*) edema of the skin limited to less than one third of the skin over the breast, (*c*) fixation of the tumor to the chest wall, (*d*) axillary lymph nodes measuring 2.5 cm. or more and proved to contain metastases, (*e*) fixation of axillary nodes to the skin or deeper structures. Haagensen also includes a less strict criterion of carcinoma developed during pregnancy or lactation.

From what sites are secondary tumors of the skull most likely to occur?

Breast, prostate, kidney (hypernephroma), and lung.

Describe an osteochondroma. Where are such growths most commonly found?

Osteochondromas are tumors formed either of hyaline cartilage or of fibrocartilage, or of both. They may be single or multiple, and are most commonly seen in the young.

Sites of Predilection: The bones, especially the phalanges, sternum, ribs, the lower epiphyseal region of the femur, the upper end of the tibia, fibula, and humerus, the scapula, the ilium, and the jaws, especially the upper.

What is an enchondroma and where are these tumors commonly found?

An enchondroma is a benign cartilaginous growth (not chondrosarcoma) found in the metacarpal phalanges, femur, and humerus. Those in the long bones often become malignant, while those in the phalanges never do.

What are gliomata and where are they found?

A glioma consists of cells containing round or oval nuclei with very little protoplasm, and fine protoplasmic extensions that interlace and form an intercellular reticulum. These tumors develop from neuroglia and more often from the white substance than from the gray. They are usually single and arise in the brain, rarely in the cord, and very rarely in the cranial nerves or embryonal rests of the nasal region.

Describe dermoid cysts. In what situations are they most commonly found?

A dermoid is a heterotopic cyst, the wall of which is composed of connective tissue lined with epithelium. The cysts contain material formed by the proliferation of the epithelium, and frequently hair, teeth, or even bone. Dermoid cysts are most commonly found in the ovary and in regions where, during bodily development, the blastodermic layers come in contact: for instance, in the neck and upper mediastinum, the eyelids, the orbital angles, the region of the coccyx, the root of the nose, and the floor of the mouth.

What are the indications for the removal of the mammary gland?

Carcinoma, sarcoma, diffuse hypertrophy, diffuse septic or tuberculous disease, occasionally multiple intraductile papillomas and, rarely, atypical hyperplasia.

Give the treatment of mammary carcinoma.

Removal of breast and axillary nodes with sternal heads of the pectoralis major and the pectoralis minor muscles (known as Halsted's operation). After the wound is healed, radiation may be given in selected cases. Oophorectomy and/or adrenalectomy and hormone therapy have a place in palliative treatment.

What is Paget's disease of the nipple? State the special significance of its occurrence.

Paget's disease of the nipple is carcinoma of the ducts under the nipple associated with an eczematoid lesion of the nipple and surrounding areola.

Describe teratomata and give their situations.

A teratoma is a tumor composed of cells, tissues, or organs, originating from more than one germinal layer. In the simpler varieties the tumor is composed of heterotopic tissues, such as bone, teeth, skin, mucous membrane, etc. The members of this group most often seen by the surgeon are branchial cysts, dermoid cysts and those of mediastinal, thyroid, or ovarian origin. The origin remains doubtful but some pathologists believe they originate from embryonal rests.

GENITOURINARY SURGERY

In what portion of the male urethra are gonorrheal strictures most common?

In the penile portion.

Differentially diagnose phimosis and gonorrhea from phimosis and subpreputial chancroid.

In phimosis and gonorrhea there is no history of a sore on the glans or prepuce; the preputial swelling is at first simply edematous; the discharge is usually purulent; there is no localized area of hardness or tenderness; chordee is frequently present; the dysuria is noted along the entire urethra; vesical symptoms are common; lymphadenitis is less frequently found than in chancroid; and gonococci are found in the discharge.

In phimosis and subpreputial chancroid there is a history of a sore; the preputial swelling is due to a localized area of hardness; tenderness is usually present; true chordee never occurs; the dysuria is experienced only when the urine comes in contact with the ulcerated foreskin; vesical symptoms are absent; and lymphadenitis is commonly found.

What are the chief affections of the scrotum?

Dermatitis, sebaceous cyst, ecchymosis, hematoma, chancre, chancroid, epithelioma, mucous patches, elephantiasis, and rarely gangrene and erysipelas.

What are the chief surgical diseases of the groin?

Inguinal hernia, femoral hernia, lymphadenitis, encysted hydrocele of the cord, tumors of the round ligament, psoas abscess, granuloma inguinale, lymphopathia venereum, and metastatic carcinoma.

What is the treatment of suppurative inguinal lymphadenitis?

Incision, drainage, and culture. Chemotherapy and biopsy of all suspicious lesions. Chancroidal adenopathies should be excised if they fail to respond to chemotherapy.

Describe hypospadias, epispadias, phimosis and paraphimosis.

Hypospadias is a malformation in which the urethra opens upon the under surface of the penis proximal to the normal position on the glans. Epispadias is a malformation in which the urethra is partially or wholly exposed on the upper surface of the penis. Phimosis is that condition in which the preputial orifice is so narrow that the foreskin cannot be retracted behind the corona. By paraphimosis is meant a strangulation of the glans penis by a prepuce which has been forcibly retracted and cannot be replaced.

What are the causes and treatment of paraphimosis?

Causes: Edema following upon the retraction of a tight prepuce.

Treatment: The glans should be rendered bloodless by digital pressure. The index and middle fingers of each hand are now crossed behind the glans, and an attempt made to force the glans through the constricted preputial orifice by pressing upon it with the thumbs. If the edema of the prepuce is very marked, injection of hyaluronidase aids in reduction. If conservative measures fail, the preputial orifice is divided by lateral incisions.

Describe exstrophy of the bladder and state its cause. Give treatment.

In consequence of an arrest in development, the posterior wall of the bladder is pushed forward by the abdominal viscera and protrudes as a red, velvety tumor. The deformity is associated with failure of the anterior abdominal wall to unite, absence of the anterior wall of the bladder, failure of union of the arches of the pubic bones, and *epispadias,* or deficiency of the roof of the urethra.

Treatment: (1) Reconstructive: Bladder is closed and epispadias repaired by plastic techniques. (2) The bladder may be excised and the urinary stream diverted by ureterointestinal anastomosis or cutaneous ureterostomy.

Describe the varieties of hydrocele.

- I. Hydrocele of the testis
  - (*a*) *Hydrocele of tunica vaginalis:* The fluid is in a sac connected with that of the tunica vaginalis.
    - 1. *Ordinary Hydrocele:* The fluid distends the closed sac of the tunica vaginalis.
    - 2. *Congenital Hydrocele:* A communication exists between the cavity of the tunica vaginalis and that of the peritoneum.
    - 3. *Infantile Hydrocele:* The tunica vaginalis and the funicular process are distended with fluid, but these are shut off from the peritoneal cavity by an obliteration placed usually at the external ring.
    - 4. *Inguinal Hydrocele:* Hydrocele in relation with a retained testis.
  - (*b*) *Encysted Hydrocele:* The fluid is in a sac distinct from that of the tunica vaginalis.
    - 1. *Encysted Hydrocele of Epididymis:* The fluid is encysted in the neighborhood of the epididymis.
    - 2. *Encysted Hydrocele of the Testis:* The fluid is encysted between the tunica albuginea and the inner surface of the tunica vaginalis.
- II. Hydrocele of the cord
  - (*a*) *Diffuse:* The fluid forms a serous collection of the nature of edema in the cellular tissue of the cord.
  - (*b*) *Encysted:* The fluid is contained in a distinct sac originating usually (1) in some unobliterated part of the processus funiculovaginalis; (2) in a cyst formed independently of this process, by dilatation of persistent tubules of the organ of Giraldés.
- III. Hydrocele of the sac of a hernia.

Give the palliative and the operative treatment of hydrocele.

Palliative: Aspiration of hydrocele fluid.

Operative: (1) The most simple method is excision of the major portion of the sac with suture or fulguration of incised edge. The scrotum is drained. (2) Doyen's method: Carefully free the hydrocele and deliver it from the scrotum, then incise it and reverse it over the testicle, excising the excess, and suture it there, in that way obliterating the cavity. The skin and hydrocele may be incised together, the edges of the hydrocele and skin sutured together, and the cavity obliterated by packing with gauze. (3) The "bottle" operation of Andrews consists in exposure of the sac of the hydrocele, opening at the neck, and inverting the sac by forcing the testicle through the opening. No sutures are required. The skin of the scrotum is closed in the usual manner with drainage.

Give the course, symptoms, and treatment of varicocele.

Course: It is an affection of early adult life, more common in the unmarried. The veins gradually increase in size if not supported by a suspensory or operated upon.

Symptoms: A dragging sensation in the scrotum; a swelling is felt along the spermatic cord resembling a bunch of earthworms; it does not give an impulse on coughing; it is almost always situated on the left side.

Treatment: Palliative: suspensory bandage. Operative: the spermatic cord is exposed in the inguinal canal and the veins are separated, preserving one or two veins with the spermatic artery. The remaining veins are divided and doubly ligated. Wear a suspensory bandage for 2 weeks.

What are the indications for castration?

Inoperable carcinoma of the prostate, bilateral tuberculosis, bilateral testicular tumors, bilateral anomalies, bilateral torsion with gangrene.

What are the causes of acute prostatitis? Describe a typical case of acute prostatitis and give the treatment.

Causes: Urethritis (usually gonorrheal), trauma, stricture, retention of urine, prostatic calculi, and cystitis.

Symptoms: Deep-seated pain, accompanied by a sensation of heat and weight in the perineum. The desire to urinate is frequent; micturition is painful, particularly at the conclusion of the act. Defecation is painful, and digital examination per rectum reveals a hot and exquisitely tender swelling of the prostate gland. Usually a mucopurulent discharge can be obtained from the urethra by massage of the prostate. The perineum is hot and tender. The patient cannot sit comfortably and supports his weight upon one buttock to avoid pressure upon the perineum. If, as is usually the case, suppuration occurs, the pain becomes more marked and of a throbbing character; the perineum becomes red and causes excruciating pain; fever is present, and there may be a marked chill. The abscess may discharge through the urethra, rectum, or perineum.

Treatment: Absolute rest in bed and liquid diet. The bowels should be kept loose to avoid the pressure of hardened feces upon the inflamed prostate. Hot hip baths sometimes cause a marked diminution of the pain. If the patient is seen early, systemic chemotherapy is usually effective. Urinary retention requires the use of a small indwelling catheter or a suprapubic cystotomy. Prostatic abscess should be incised and drained either transurethrally or transperineally.

Give the symptoms, diagnosis, and treatment of vesical outlet obstruction.

Symptoms: These vary from mild urinary frequency and nocturia to complete retention of urine. Characteristically, the urinary stream is weak and of diminished caliber. There are difficulty in initiating the stream and postmicturition dribbling. The bladder cannot be emptied completely and residual urine collects, predisposing to cystitis and upper urinary-tract infection. Gross or microscopic hematuria are common symptoms.

Diagnosis: Rectal palpation of the prostate may reveal enlargement of the gland. Endoscopy may be required to confirm obstruction occurring with a smaller fibrous gland. Residual urine should be measured and cultured.

Treatment: NONOPERATIVE: Warm sitz baths and chemotherapy may improve selected patients.

OPERATIVE: (1) Transurethral resection, (2) suprapubic enucleation, (3) retropubic enucleation, (4) perineal enucleation or prostatectomy.

What examinations should precede any operation upon the prostate?

(1) Complete physical examination, (2) hemoglobin and white blood cell determinations, (3) urinalysis, (4) intake and output of fluid, (5) blood urea nitrogen estimation or nonprotein nitrogen, (6) phenolsulfonphthalein test, (7) urogram.

Describe the operation of perineal prostatectomy.

The patient is placed in exaggerated lithotomy position. A sound or curved

Lowsley tractor is passed to the bladder. An inverted "U" incision is made in the perineum, the central tendon is divided, and the rectum is reflected posteriorly. Denonvillier's fascia is incised and the gland exposed. The urethra is opened near the apex of the glans, a straight tractor is introduced, and with this as lever and traction, the adenoma is enucleated. Insert a Foley catheter into the bladder. Hemostasis is obtained by suture ligations, and the capsule and skin are closed.

Describe the operation of suprapubic prostatectomy.

One or two stages. Two stages are indicated if the bladder is atonic, or the patient's general condition prohibits the one-stage procedure. Stage I consists of suprapubic cystostomy, leaving a large caliber tube for drainage. At the second stage, or at a one-stage procedure, the bladder is exposed extraperitoneally through a midline or transverse suprapubic incision. The bladder is opened and its interior inspected. The mucosa overlying the prostate is incised, a finger introduced into the prostatic urethra and a cleavage plane found anteriorly. The lobes are enucleated. Hemostasis is secured by suture ligations at the bladder neck. A Foley urethral catheter is placed and Foley or mushroom cystostomy tube.

What operations are considered best for the relief of prostatic obstruction?

Most urologists agree that small fibrous glands, small- to moderate-sized adenomas, and obstructive incurable carcinomas of the prostate are best treated by transurethral resection. Larger adenomas are removed suprapubically (transvesically), retropubically, or perineally. Carcinoma confined to the gland is best treated by radical excision through either the perineal or retropubic approach.

Discuss the treatment of postprostatectomy urinary tract infections caused by Pseudomonas aeruginosa.

Unfortunately, most strains of Pseudomonas aeruginosa are naturally resistant, or relatively so, to most of the antibiotics, except polymyxin B. Because of the toxic reactions associated with this antibiotic, its clinical usefulness is limited. However, a new polypeptide antibiotic, colistin (Colymycin) has recently been used successfully in the treatment of antibiotic resistant pseudomonas infections involving the urinary tract. Since colistin is not absorbed from the gastrointestinal tract, it is necessary to administer the drug parenterally—in most such infections an average dose of 2.5 mg./kg./day, given in 2 to 4 divided doses intramuscularly for five days has been effective.

Define nephropexy, nephrotomy, and nephrectomy. Give the indication for the performance of each.

Nephropexy is the suturing of a kidney into a more desirable position. Indication: following the correction of ureteropelvic anomalies or plastic procedures on the kidney.

Nephrotomy is the cutting into a kidney. Indication: renal calculus or biopsy.

Nephrectomy is the excision of a kidney. Indication: a primary malignant renal growth, advanced destruction secondary to infection or calculus, congenital anomalies, and in selected cases of hypertension with unilateral renal disease.

Describe the operation of nephrectomy.

Nephrectomy may be performed through the translumbar, transperitoneal, or transthoracic approaches. The usual method is translumbar. The patient is placed in the lateral position, with the dependent costal margin elevated. The retroperitoneal space is entered through an incision paralleling the 12th rib or through its bed. Gerota's fascia is entered or dissected free (in neoplasms). The ureter is divided between clamps and doubly ligated. The renal vessels are handled in a similar fashion, the kidney is removed, and the wound closed in layers, usually with drainage.

Give symptoms of stone in the kidney and treatment of same.

Symptoms: The patient usually complains of pain in the loin, and sometimes of pain in the iliac fossa. Deep percussion over the kidney causes pain in the loin. Pain is aggravated by exercise. The urine often contains albumin and blood. Frequent micturition may be noted. The urine may be purulent. Renal colic may occur owing to obstruction of the collecting system by the calculus. An intravenous urogram is an essential study.

Treatment: The symptoms can be treated by hypodermic injections of morphine and atropine or their substitutes. A hot bath is sometimes helpful. If infection is present, antimicrobial therapy should be instituted. Operative treatment is indicated if the stone causes complete obstruction, severe pain, persistent infection, or persistent hematuria.

Give the diagnosis, causes, and treatment of rupture of the urinary bladder.

History of trauma, bloody urine, or retention of urine, signs of extravasation of urine. Absolute diagnosis is made by the detection of radioopaque material outside of the bladder after a cystogram. Rupture of the apex of the prostate gland can also be demonstrated by a urethrogram. A presumptive diagnosis of rupture in this area is made if a catheter cannot be introduced into the bladder. If the diagnosis is doubtful, exploration is indicated.

Predisposing Causes: Distention of the bladder, ulceration, and degeneration.

Exciting Causes: Obstruction to outflow of the urine (by stricture or enlarged prostate); external violence; lifting; straining at stool, during micturition, or parturition; forcible injection of the bladder; instrumentation; perforation by missiles.

Treatment: In extraperitoneal rupture, drain the perivesical space and divert the urinary stream by cystostomy. In intraperitoneal rupture, expose the bladder, suture the opening in the bladder, and divert the urinary stream.

What are the causes of atony of the bladder?

Neurogenic, chronic overdistention from obstruction, acute overdistention, and senility.

Describe the treatment for acute retention of urine.

In retention due to organic stricture, dilate the stricture if possible and leave a catheter indwelling. If this is impossible, divert the urinary stream proximally (urethrostomy or suprapubic cystostomy). If the obstruction is at the bladder neck, dilatation is usually impractical.

Name the principal operations for stone in the bladder.

Litholapaxy, suprapubic lithotomy, and perineal lithotomy.

Describe suprapubic lithotomy.

The bladder is filled through a catheter, exposed extraperitoneally through a suprapubic incision, opened, and the stone (or stones) removed. The bladder may be closed primarily or drained by cystostomy tube.

Outline the management of a patient with ureteral calculi.

Palliative: Morphine and/or its derivatives can be given for pain. Banthine (100 to 150 mg. i.v.) is often of value. Hot baths, plenty of fluids and chemotherapy if fever and/or pyuria are present are indicated. Intravenous urogram should be made to determine status of renal function, degree of obstruction, confirm presence of stone.

Nonoperative Management: Many calculi of small size (under 5 mm. in diameter) may pass spontaneously after a few colics. Repeated severe attacks of colic, persistent fever, hematuria, and obstruction may necessitate (*a*) or (*b*):

(*a*) URETERAL MANIPULATION: Under anesthesia, a looped catheter or stone basket is passed cystoscopically to engage the stone in the ureter and withdraw it.

(*b*) URETEROLITHOTOMY: The ureter is exposed retroperitoneally in the proper area, incised longitudinally over the stone, the stone removed, and the wound closed in layers with drainage.

What are the symptoms and how do you diagnose a stone in the bladder?

Symptoms: Frequency, dysuria, intermittent obstruction of urinary stream; hematuria is common and there is pyuria.

Diagnosis: History, rectal palpation, detection by contact with a sound, visualization by endoscopy and by x-ray.

Give the diagnosis and treatment of complete rupture of the membranous urethra.

The symptoms of rupture of the urethra are considerable pain aggravated by motion, pressure, and attempts to pass urine. In some cases micturition is still possible. If so, blood precedes and also discolors the urine. The presence of a large swelling is regarded as evidence of urethral rupture. In rupture of the membranous urethra, if uncomplicated, the urine remains between the two layers of the triangular ligament until this space is filled, and then passes up on the anterior abdominal wall.

Describe an operation for circumcision.

The prepuce is retracted if possible and adhesions between foreskin and glans broken up and the smegma removed. The prepuce is pulled forward again and the level of the corona marked by a transverse incision. Removal of the skin distal to this is accomplished by sharp dissection or by cutting at this level proximal to a clamp applied after the glans is retracted. The mucous membrane is then trimmed to within 3 to 4 mm. of the corona. Hemostasis is secured by ligatures and the skin and mucous membrane edges approximated by fine plain catgut sutures.

What is the usual site of a vulvovaginal abscess? Give the symptoms and treatment.

The glands of Bartholin.

Symptoms: Heat, redness, tenderness, and local swelling. In the early stages, this swelling is best detected by introducing the finger in the vagina and pressing outward.

Treatment: Incision and drainage. The wound should be packed with gauze and dressed daily until healed.

RECTAL SURGERY

Name the most common varieties of fistula.

Fistula in ano, vesicovaginal, urethrovaginal, rectovaginal, perineal, salivary, biliary, bronchopleural, tracheo-esophageal, gastrocolic, and intestinal.

Describe the signs of fistula in ano.

The fistula has an external opening in the skin and an internal opening in the bowel. The external opening is usually situated within 1 inch of the anus; the internal opening is generally within 1 inch of the margin of the anus, most frequently immediately above the sphincter. The escape of fluid feces and flatus through a complete fistula is common.

How would you treat a fistula in ano?

The bowel should be completely evacuated by an enema at least an hour before the operation. The patient is anesthesized and placed in the lithotomy position or full prone position with the pelvis elevated and the perineal and anal regions are shaved and properly cleansed. The external sphincter is gently stretched with the thumbs in the rectum; a grooved director is then passed into the external orifice of the fistula and through the fistulous tract into the bowel. A curved bistoury is now introduced along the grooved director, and all the overlying tissues are divided. The tract may also be excised. All pockets and tributary branches of the fistula must be opened up and curetted, but the internal sphincter is not cut in more than one place. Multiple fistulous tracts sometimes necessitate the use of a seton of silk to identify the remaining tracts for secondary excision. All undermined tissue and unhealthy tags of skin should be removed. Hemorrhage should be checked, the cavity carefully packed with gauze, and compression made over the anal region by a thick pad of sterile gauze and a T-binder.

What are the causes of ischiorectal abscess?

Predisposing causes: tuberculous and pyogenic infections, ulcerative colitis. *Exciting causes:* trauma, fissure, and fistula in ano.

Give symptoms and treatment of acute ischiorectal abscess.

The symptoms are the same as those of an abscess, the swelling, however, being brawny, and fluctuation may be difficult to detect. Pain is often noted in the groin and there may be enlarged glands in this region.

Treatment: Immediate incision over the point of fluctuation and as near to the anus as possible so that the opening of a resulting fistula will be close to the anus. It may be linear, circular, T-shaped, etc., depending upon the area to be drained and preference of the operator. Incision is followed by insertion of the finger, breaking down the necrotic septa of cellular tissue, irrigation, and packing with gauze.

To what are hemorrhoids due? How many forms are described? How are they treated?

Hemorrhoids may be caused by anything that induces passive congestion in the pelvic circulation, such as pregnancy, malignant disease, cirrhosis of the liver, constipation, certain occupations, etc. Hemorrhoids may be external or internal, according as they are situated above or below the sphincter ani.

Treatment: Internal hemorrhoids, if small, have been reported to disappear by the injection of some antiseptic and astringent fluid (such as phenol in oil). If they are large or external, the hemorrhoids must be removed surgically by excision and ligation of the veins. *External* hemorrhoids are always removed surgically. Prior to the treatment of any hemorrhoids, a sigmoidoscopic examination should be performed to exclude the presence of a carcinoma of the rectosigmoid.

Describe an operation for the removal of hemorrhoids.

With the patient anesthesized, prepared, and in proper position, the lubricated index finger is inserted to lubricate the anal canal. A retractor is inserted, and the anus inspected to determine the tissue to be removed. A curved hemostat is applied to each primary hemorrhoid to include just the amount of tissue to be excised with the tip of the forceps at the apex of the hemorrhoid. Each hemorrhoid is ligated with a suture ligature of chromic catgut at the tip of the hemostat, and elliptical radial cuts are made in the skin and mucous membrane adjacent to the hemorrhoid. The hemorrhoid is freed from its bed, exposing the sphincter fibers. Arterial bleeding in the bed is controlled with ligatures or suture ligatures. Each hemorrhoid is cut away at the point of the hemostat, leaving sufficient tissue so that the primary ligature does not slide off the end. The edges of these elliptical incisions may or may not be sutured together; both methods have advantages, but closing the mucosa and leaving the skin incisions open is less apt to produce a stricture.

Give the symptoms and treatment for carcinoma of the rectum.

Symptoms: Bleeding is the most frequent early symptom. The blood is frequently mixed with mucus and pus. Ulceration of the tumor may produce irritation of the bowel with tenesmus and a desire for frequent defecation. There may be constipation and alteration of the normal bowel habit. Pain is a very late symptom. Chronic intestinal obstruction may develop slowly. Urinary symptoms develop when the lesion lies against or involves the bladder.

Treatment: Removal of the growth and the lymphatic lines of extension by a combined abdominoperineal operation or a modification of it. Colostomy or cecostomy may have to be performed as a preliminary procedure.

What are the causes of stricture of the rectum?

They are divided into congenital and acquired. There are two forms of acquired stricture. The first variety is due to external pressure, caused by adhesions or a growth. The second form may be caused by syphilitic, tuberculous, or dysenteric ulceration, cicatrices after local inflammation, operation, trauma, rectal gonorrhea, and lymphopathia venereum, particularly in Negro women.

EYE, EAR, NOSE, AND THROAT

Give (1) the causes, (2) symptoms, and (3) treatment of acute iritis.

(1) Syphilis, rheumatism, diabetes, trauma, infection, gonorrhea, smallpox, septicemia, typhoid fever, pneumonia, and tuberculosis.

(2) Pain in the eye and forehead, lacrimation and photophobia, dimness of vision, unequal pupils, cloudiness of the aqueous humor, punctate deposits in the posterior surface of the cornea, change of color of the iris, and injection.

(3) Atropine, 1 or 2 per cent aqueous solution; ethyl-morphine (Dionin), 1 or 2 per cent; warm moist compresses; foreign protein therapy; and supportive measures, such as bed rest, protection from light, and removal of foci of infection. In specific cases, specific therapy is indicated locally and systemically.

Describe the local effects produced by a solution of atropine sulfate and pilocarpine hydrochloride, when dropped into the eye. What strength of the solution of each would you prescribe for the usual purposes for which they are used? What are the contraindications to the use of each?

Atropine dilates the pupil, paralyzes the muscles of accommodation, prevents the formation of adhesions of the iris and cornea and may break them up when they have already formed, encourages stasis by dilatation of capillaries, relaxation of ciliary muscle, and collapse of the veins of the choroid. Pilocarpine contracts the pupil and decreases vascular engorgement.

Atropine sulfate, 1 or 2 drops of a 1 per cent solution. Pilocarpine hydrochloride, 1 or 2 drops of a 1 per cent solution.

Contraindications: Atropine: glaucoma and any condition with increased intraocular tension. Pilocarpine: weak heart and ptyalism.

What muscles are divided in the operation for (a) diverging strabismus; (b) converging strabismus?

(*a*) The external rectus; (*b*) the internal rectus.

What is glaucoma? Give the treatment of glaucoma.

Galucoma is a disease of the eye characterized by increase of intraocular tension, excavation of the optic disk, restriction of the field of vision, corneal anesthesia, colored halos about lights, and a diminution of vision that may become absolute.

Treatment: Iridectomy, alone or combined with trephining of the cornea. Eserine is used after operation.

What is a cataract? What are some of the etiologic factors in the development of cataract? Outline a plan of treatment of cataract.

A cataract is an opacity of the crystalline lens.

Etiological factors are diabetes, parathyroid insufficiency, senile changes, trauma, general diseases, chemical poisoning, ocular diseases, and certain occupations that involve exposure to intense heat or intense light.

Treatment: Accurately determine the amount of vision in the sound eye; radical surgery at the optimum time determined by the surgeon; perform extraction of the lens either in one stage or after preliminary iridectomy, or extraction of lens combined with iridectomy. Prescribe corrective glasses.

Mention some of the causes of detachment of the retina.

Myopia of high degree, high blood pressure, sudden increase in tension, trauma, infection, iridocyclitis, nephritis, toxemia of pregnancy, choroidal hemorrhage, exudate, and tumor.

Describe briefly the procedures for obtaining reattachment of the retina.

Operative procedures are directed toward closing the retinal tear or creating a line of adhesive choroiditis around the hole in the retina or entire area of detachment. Under local anesthesia a conjunctival flap is turned back, and the insertion of a rectus muscle or two divided. The edges of the opening or detachment are scarred by electrocauterization, diathermic coagulation, or electrolysis.

Outline the treatment of acute conjunctivitis.

Remove the cause. Instill specific antibiotic solution or ointment. Symptomatic treatment consists of rest, antiseptic or astringent solutions, and irrigations (boric acid 10 gm. to 500 cc. water, t.i.d.), cold compresses, and ophthalmic ointment.

What special precaution must be taken in the management of a case of gonorrheal ophthalmia?

Protection of the unaffected eye by wearing a glass shield. Explain carefully to the patient the nature of his disease and impress upon him the necessity for protecting the sound eye. He should lie on the affected side. Early cold applications should be used continuously and the eye irrigated with boric acid solution. Atropine should be instilled. Penicillin irrigations and penicillin ophthalmic ointment should be used in conjunction with massive doses systemically. If a panophthalmitis develops, perform enucleation in order to save the sound eye from sympathetic ophthalmia.

What are the indications for iridectomy?

Prolapse of the iris following perforated wounds of the cornea; as a preliminary to the extraction of a cataract; for relief of tension in glaucoma, foreign bodies, tumors of the iris, or corneal scarring or fistulas.

What measures should be instituted in order to prevent serious complications following removal of a foreign body imbedded in the cornea?

Wash the eye out with warm boric acid solution; keep the pupil dilated with atropine for at least 24 hours; apply patch; always see the patient daily for at least 72 hours. Antiseptic ointments are probably helpful.

What are the causes of ptosis and the remedial measures employed?

Paralysis of the oculomotor nerve, cortical lesion in the brain, fracture of the skull, syphilis, rheumatism, congenital malformation, injury or paralysis of the levator palpebrae muscle, trachoma, or tumor of the lid. Paralysis of cervical sympathetic ganglia on the same side gives apparent ptosis.

Treatment: Appropriate constitutional treatment. In the absence of constitutional causes, operations are performed to increase the action of the frontalis muscle upon the upper lid. If the action of the levator muscle is not entirely lost, the muscle may be shortened. Action of superior rectus may be utilized. A strip of tarsus may be excised.

What are the indications for enucleation of the globe?

Malignant disease, either primary or extending from adjacent tissues; rupture and collapse of the eyeball; a large, irregular foreign body in the eye not susceptible of being successfully removed; a large wound in the dangerous region when little hope of obtaining useful sight remains; a small foreign body not removable by the electromagnet and causing inflammation and shrinking of the eyeball; a corneal wound in which severe iritis and panophthalmitis develop in spite of treatment; and any case in which sympathetic ophthalmia is threatened.

Describe enucleation of the eyeball.

The conjunctiva near the cornea is grasped with forceps and divided with scissors entirely around and close to the corneal margin. The recti muscles are now caught up separately with a strabismus hook, and their tendons divided close to the ball. Scissors are passed back in the orbit until they touch the optic nerve, when their blades are opened and the nerve divided as far back as possible. The oblique muscles and other remaining tissues are now quickly divided and the hemorrhage checked. The four recti muscles are sutured together and the wound packed with gauze and, preferably, a sphere placed in the orbit.

What is treatment for stenosis of the lacrimal duct?

Slit the lower canaliculus inward and slightly upward on the conjunctival surface. Follow this by dilatation with Bowman's probes. The dilatation will be required every few days for several months.

What is milium? Give the treatment.

Milium is an affection characterized by the appearance of small, pearly, noninflammatory elevations upon the edges of the eyelids. They result from blockage of the ducts of sebaceous glands.

Treatment: The lesion should be incised and the contents removed.

Describe the nonsurgical and the surgical treatment for chronic sinusitis.

Nonsurgical: Secure ventilation and drainage by contraction of the turbinates, by use of vasoconstrictor drugs combined with systemic antibiotics. General supportive treatment by adequate diet and fluid intake. Correction of anemia if present. Steam inhalations. Change in climatic environment.

Surgical: Exposure of the sinus by open operation, followed by removal of the entire mucous membrane and the provision for permanent drainage into the nose.

What are the indications for the removal of the tonsils?

Recurring attacks of tonsillitis or peritonsillitis or hyperplasia of the tonsillar tissue with airway obstruction.

Describe tracheotomy.

Tracheotomy is the formation of an external opening into the trachea. The opening may be made either above or below the isthmus of the thyroid, the high operation being usually preferred. Always use local anesthesia. The incision is made in the median line from the cricoid cartilage 1½ inches downward, exposing the isthmus of the thyroid gland. This is drawn downward with a blunt hook or, if necessary, divided, the trachea steadied with a sharp hook, and the first two or three rings divided from below upward. Venous hemorrhage may be disregarded, for it will cease after the first few respirations through the tracheal wound. A tracheal cannula is at once introduced and secured with tapes.

Indications: Tracheotomy is indicated

for upper airway obstruction, excessive secretions in the lower airway that require repeated aspiration when the patient cannot clear voluntarily, and as a preliminary procedure to certain types of oral surgery.

Give the symptoms and treatment of acute mastoiditis.

Symptoms: Pain and tenderness over the mastoid, edema with pitting over the same area, temperature 100° to 104°F., rapid pulse, and chills occasionally. Deafness and discharge are frequently present.

Treatment: Systemic antibiotics in adequate doses, along with hot applications over the area and general systemic treatment. Free incision of the eardrum should be done. In a few cases, the symptoms may persist over several weeks or may extend to the periosteum or cause meningeal irritation. Then a simple mastoid operation should be performed. Fluids and transfusions are given as indicated.

Describe an approved method for the removal of impacted cerumen.

The external auditory meatus should be syringed with hot water; if this does not remove it, drop in a small amount of a solution consisting of equal parts of hydrogen peroxide and water, to which a small amount of bicarbonate of soda has been added; allow it to remain 5 minutes, then renew syringing.

Can deafness be helped with surgical procedures?

Yes, but only conductive deafness. Such patients may be helped by mobilization of the stapes or by fenestration.

Name the methods of inflating the tympanum.

Valsalva's maneuver, Politzer's bag, and the eustachian catheter.

What are the reasons for incising the membrana tympani?

The evacuation of serum, pus, or mucus from the tympanic cavity and the relief of anomalies of tension of the drum membrane.

Outline the treatment of acute purulent otitis media in the early stage.

Antibiotics are given in adequate dosage as indicated. Heat locally, sedation, and glycerine with antipyrene or 2 per cent phenol are used to relieve pain. Treatment of other primary nasopharyngeal foci of infection should be carried out. Myringotomy is performed for bulging of the drum membrane with diminished hearing and severe pain. The most favorable location is the postero-inferior quadrant.

Give the causes and sequelae of suppurative middle ear disease.

Causes: Infection from the nasopharynx through the eustachian tube, infection through perforations of the membrana tympani, and, rarely, through the blood vessels or lymphatics.

Sequelae: These may be divided into the extracranial, cranial, and intracranial.

Extracranial: eczema of the meatus, furuncles of the meatus, and necrosis of the tympanic plate. Cranial: necrosis of the ossicles, necrosis of the temporal bone, facial paralysis, and mastoiditis. Intracranial: extradural abscess, meningitis, thrombosis of the lateral sinus, and brain; deafness may be a result of several factors.

Give treatment for malignant neoplasms of the nasopharynx.

The treatment, whether carcinoma or sarcoma, is irradiation. Surgery, other than for biopsy, should not be attempted.

COMPLICATIONS OF SURGERY

Discuss the physiology of circulatory shock.

Circulatory shock is a condition in which the cardiac output is so greatly reduced that tissues throughout the body begin to deteriorate. Any circulatory abnormality that greatly reduces the cardiac output can cause circulatory shock. These include: (1) cardiac shock in which the cardiac output often falls very low; (2) hypovolemic shock, which results from greatly reduced blood volume caused by blood loss, plasma loss, or dehydration; and (3) neurogenic shock that results from sudden inhibition of the sympathetic nervous system throughout the body. This allows all of the systemic vessels to dilate and the blood to "pool" in the lower part of the body instead of returning to the heart.

Define shock and give the clinical signs of severe shock.

Shock is a loosely used term most commonly used to designate a clinical syndrome characterized by inability of the circulating blood volume to fill the available vascular bed.

The patient has a low blood pressure and weak pulse with a fast rate; his extremities and face are cold, pale, and moist. Restlessness and the symptoms of dyspnea are characteristically found. Less severe shock may show variations, which range to hypertension, warm extremities, and/or normal pulse.

What is the treatment for shock in a surgical patient?

Hemorrhage is controlled and the blood volume restored by blood, plasma, or plasma expanders, by rapid infusion if necessary. Oxygen in high concentrations should be administered. Pain and restlessness can be controlled by morphine. Large doses should be avoided, since they may further depress the blood pressure. Vasoconstrictors, i.e., epinephrine, Vasoxyl, Neo-Synephrine, etc., may be of temporary benefit. Excision of devitalized or crushed tissue may be necessary. Normal body temperature should be maintained and concomitant infections treated specifically.

Discuss the problems involved with transplantation of tissues.

The transplantation of tissues or organs from one person to another is principally a problem of immunity. The new host may either already be immune to the transplanted tissue, or he may develop immunity within a few weeks' time, which then causes death of the cells of the transplant. For this reason, successful transplantation of organs that contain living cells can usually be achieved for only a few weeks. The one exception to this occurs in identical twins, who also have identical patterns of antigens in their cells and, therefore, will not develop immunity against the transplant. Very frequently, noncellular tissues, such as dead bone, tendon, fascia, and cornea of the eye can be transplanted without subsequent destruction of the tissue. In these instances it is only the extracellular tissue that survives. In view of the above disadvantages associated with the transfer of tissues, the trend toward the use of synthetic prostheses has grown. For example, Dacron and Teflon are currently the favorite synthetic materials, and satisfactory prostheses have been fabricated in weave, knit, and braid as blood-vessel substitutes.

What is the normal sequence of physiologic changes during surgical convalescence?

There are a number of well-recognized responses of the body to trauma. These are divided by Moore into four phases:

(1) The adrenergic-corticoid phase, which in young patients lasts from 1 to 7 or more days, depending upon the degree of trauma. The patient has some degree of tachycardia, peripheral vasoconstriction, relative oliguria, anorexia, and hypoactive or absent peristalsis. He loses weight, has a large excretion of urinary nitrogen and potassium, retains sodium, has a low total eosinophile count, and an initial high excretion of 17-ketosteroids.

(2) The corticoid withdrawal phase follows the adrenergic-corticoid phase and lasts 2 to 3 days. Peristaltic activity increases, flatus is expelled, and appetite improves, and the patient has increasing interest in his surroundings but very little stamina. The wound shows fibroblastic and epithelial proliferation and increased tensile strength. There is further weight loss but with less nitrogen excretion and definite diuresis and often decrease in the total body water. Urinary potassium excretion is low and sodium excretion increases. The caloric intake increases and the total eosinophile count may be high.

(3) The spontaneous anabolic phase is dependent upon adequate dietary intake and the patient has an unusually large appetite and increased physical stamina (but still below his expectations); but sexual and menstrual function remain subnormal. The wound continues to heal with increase in tensile strength. Gain in weight is noted. There is a consistently positive potassium and nitrogen balance with a zero sodium balance. The total eosinophile count is normal but the excretion of 17-ketosteroids remains subnormal. Total body water increases.

(4) The fat gain phase may last for months and is characterized by the patient's regaining normal physical stamina and activity. The color of the wound changes from red to white and the wound flattens somewhat. Total body water remains constant but weight increases. Other metabolic activities return to normal.

The endocrinological and other controls of these processes remain under investigation and are not fully documented.

List the possible complications associated with aortic grafts.

(1) *Thrombosis:* Occasionally, manipulation of a very atheromatous aorta or application of clamps has produced either an embolus or a thrombosis of the femoral-popliteal arteries.

(2) *Hemorrhage:* This can occur as a result of poor vascular technique in effecting the anastomosis and is a common sequel of regional infection. Significant blood loss rarely occurs through the currently used synthetic prostheses.

(3) *Infection:* This is serious in the presence of either homograft or synthetic replacement (in the former, rupture and fatal hemorrhage are common). For complete obliteration of the infection, it is usually necessary to excise the graft, since it acts as a foreign body.

(4) *Renal Failure:* This complication is most frequently a sequel of treatment of ruptured aneurysms. It was more common in the early years of excisional therapy when the operating time was extended and many units of blood were used at the time of surgery.

(5) *Duodenal Fistula:* In some very large abdominal aortic aneurysms, the third portion of the duodenum is not only extremely adherent but is stretched across the anterior surface of the sac. After the dissection of this from the sac, a subsequent duodenal fistula may develop, a serious complication.

(6) *Ureteral Trauma:* The danger to the ureter arises from the surgical dissection, especially near the origin of the left common iliac vessels, since the ureter may become adherent to the posterior lateral aspect of the sac.

(7) *Central Nervous System Damage:* With the manipulation and dissection involved in excising aneurysms of the ascending thoracic aorta, or aortic arch, there is a real danger of embolization to the brain or peripherally.

What are some of the physiologic changes during hypothermia?

Oxygen consumption steadily declines with the fall in body temperature if shivering is controlled. The blood pressure falls and the cardiac rate and output decrease. Venous pressure rises slowly. Serum potassium probably decreases, while the pH of the blood varies depending upon the alveolar ventilation. The clotting time appears to be progressively prolonged. Kidney function is reduced. The electrocardiogram shows a slurring and notching of the R wave and flattening and inversion of the T wave. Ventricular fibrillation is more easily induced. Survival of ischemic tissue is increased.

How should cardiac arrest be treated?

If recognized promptly, the heart should be massaged, preferably through an incision in the left fifth intercostal space and the open pericardium. A clear airway should be established immediately and controlled respiration maintained. If ventricular fibrillation should occur, electrical shock of approximately 220 volts for one-tenth second is usually effective in stopping fibrillation. Calcium chloride, epinephrine, and molar sodium lactate are helpful in selected incidences. The underlying cause of the arrest should be corrected whenever possible.

Give the indications for the performance of blood transfusion.

The administration of compatible blood is indicated: (1) for loss of blood by hemorrhage; (2) in shock when there is a deficiency of circulating fluid; (3) in infections when immune bodies are needed; (4) in blood dyscrasias in which a deficiency of certain cells exists; (5) in nephrosis or other hypoproteinemias when blood proteins are needed; (6) in conditions of anemia or altered hemoglobin in which active hemoglobin is needed; and (7) in hemorrhagic states when coagulative factors are needed.

Section 9

OBSTETRICS AND GYNECOLOGY

OBSTETRICS

Trace the life history of the human ovum from inception to fertilization.

The progenitors of mature ova are the primary oocytes. They are formed in the young embryo and throughout the functioning life of the ovary. At birth, there are thousands of oocytes in the ovarian cortex. They derive from two sources: large epithelioid cells in the primitive coelomic peritoneum; and cells of the germinal epithelium, which cover the ovary. These cells migrate from both sources into the primitive ovarian cortex, where they divide rapidly to form the oocytes. The ova that are formed later, during the functioning life of the mature ovary, originate from the germinal epithelium. Each young ovum is surrounded by a single layer of special cells soon after its formation. This unit of an ovum and the cells that surround it (granulosa cells) is called a "primordial follicle." The granulosa cells will manufacture the first ovarian hormone, estrogen.

When adult sex life is established, one ovum and usually only one is prepared for fertilization during each menstrual cycle. Not only the ovum but also the follicle in which it is contained undergo elaborate changes before the ovum is ready for conception and subsequent implantation. At the beginning of each normal, mature, menstrual cycle, a number of primordial follicles develop and migrate toward the ovarian surface. This is in response to the follicle stimulating hormone (FSH) of the anterior pituitary gland. The granulosa cells of these stimulated follicles divide rapidly and secrete estrogen, which accumulates in the central portion of the granulosal mass. This converts the follicle into a cyst. Each ovum projects into its central cystic space in a small mound of granulosa cells, the cumulus oophorus.

One of the maturing follicles finally distends the ovarian surface and soon thereafter ruptures through it. The follicular contents, including the egg and its surrounding granulosa cells, the corona radiata, are extruded into the peritoneal cavity. This occurrence is ovulation. The other stimulated follicles stop growing and atrophy. These regressing follicles are called "atretic follicles." They finally become nothing but a small, round, white scar, a corpus albicantia. Shortly before the egg of the particular cycle is extruded, it undergoes the first of two maturation divisions that are necessary to prepare it for fertilization. The first division is unique in that it halves the total chromosomal number. Normally, the chromosomal content of the human cell is 22 paired chromosomes plus one pair of sex chromosomes, which may or may not be paired. The total number of chromosomes is, therefore, 46, the so-called diploid chromosomal number. The first maturation division splits the cell and its nucleus into two parts, each nucleus containing only one half of the normal number of chromosomes. This half number, 23, is called the haploid number. Only one of the two segments that result from the division is of value and the useless half, a polar body, is cast off and dies. The maturing ovum must still undergo a second maturation division before it is ready to be fertilized. It occurs after ovulation and usually in the distal fallopian tube. It is a normal division and maintains the haploid chromosomal number. Again a useless polar body is formed and discarded.

Define and describe conception.

Conception, or fertilization, is the union of an ovum and a spermatozoon, each of which has been prepared by two maturation divisions and has a haploid number of chromosomes. The result is a fertilized egg. This occurrence usually takes place in the outer portion of the fallopian tube within hours of ovulation and usually within hours of intercourse. The maturing ovum bursts into the peritoneal cavity surrounded by its adherent granulosa cells, the corona radiata. It enters the tube, guided by a current of peritoneal fluid that is developed by the ciliary action of cells lining the fimbria of the tube and the endosalpinx. To increase the probability of the egg's entering the tube, the distal tube reaches out toward the ripening follicle and the fimbria practically engulfs the area from which the egg will escape. This purposeful action of the tube is not essential, however, as is proved occasionally by an ovum's migrating from one ovary through the peritoneal cavity to the contralateral tube. Once the egg is in the tube, it is propelled through it toward the uterus by tubal peristalsis and ciliary activity. The tubal peristalsis is a response, in part, to the mass within the tubal lumen and in part to the effect of ovarian hormones. The spermatozoa, which are deposited in the upper vagina by intercourse or artificial insemination, pass rapidly through the cervix, into the uterine cavity, and out through the tube. Although the whipping action of the spermatozoal tail contributes to its transportation, muscular activity of the uterus and tube play an important role in the migration. The time of travel is too short to be explained solely by the activity of the spermatic tail. Many spermatozoa surround the ovum as it moves through the tube. The head and neck of one of them finally enter the egg and immediately the ovular cover becomes impermeable to the other spermatozoa. The process by which the spermatozoon enters the egg is unknown. It may be inherent in the egg or in the spermatozoon. The head of the spermatozoon becomes the male pronucleus, the tail, a centrosome. Fusion of the male pronucleus with the female pronucleus (the ovular nucleus) restores the normal diploid chromosomal number. The cell that has been formed by this union is the fertilized egg and this process, by which the fertilized egg has come into being, is fertilization. If the spermatozoon has added an "X" sex chromosome to the "X" of the ovum, the child will be a girl; if it has added a "Y," it will be a boy.

Describe the migration of the fertilized ovum.

The fertilized egg divides repeatedly during its 3-day migration through the tube to the uterine cavity, but it does not increase in diameter. This is because its volume is restricted by the inelastic zona pellucida that surrounds it. The cells of the corona radiata degenerate en route or are dispersed by the tubal movement. The products of their degeneration and the secretions of the tubal and endometrial mucosa nourish the egg until implantation. Upon entering the uterine cavity, the egg floats freely and it continues to do so for several days. The zona pellucida ruptures and the ovular diameter increases rapidly. Then, some 6 to 10 days after conception, the ovum settles on the endometrium and begins to burrow into it. This process is termed "implantation." The endometrium, now that pregnancy exists, is renamed the decidua. The site of implantation is most commonly high on the anterior or posterior uterine wall.

Describe briefly early ovular development.

Soon after fertilization and the fusion of the two pronuclei and their surrounding cytoplasm, the fertilized egg divides normally, the first of a continuing series of normal divisions. Each daughter cell normally has the same 46 chromosomes as the mother. The mass of undifferentiated cells that comprise the embryo during tubal migration looks like a mulberry and is called a "morula." About the fourth day, cellular differentiation is apparent, and the embryo, now in the uterus, is termed a "blastula." First the ectoderm and entoderm are distinguishable, then the mesoderm. A liquid-containing space, the exocoelom, splits the ectoderm, and the embryo becomes a blastodermic vesicle. The ectoderm surrounding this cavity—and the entire embryo—is the ectodermic chorion. It will receive a lining of somatic mesoderm. Meanwhile, a mass of ectoderm, splanchnic mesoderm, and entoderm protrude at one pole into the developing central space of the blastodermic vessel. This cell mass will develop into the fetus and is called the "inner cell mass." It is at this stage that implantation usually occurs.

Name and identify the three types of decidua.

"Decidua" is the name given to the endometrium of pregnancy. The decidua basalis is that part of the decidua lying directly beneath the developing ovum. It contributes the maternal portion of the placenta. The decidua capsularis is the decidua that was the roof of the ovular space. It stretches over the growing egg and atrophies along with the chorion laeve with which it is in contact. The decidua vera is the remainder of the decidua. The junction of the decidua basalis and capsularis is marked by a gross thickening, which results from fibrinous degeneration of chorionic ectoderm. This raised circumference of the placenta is named the closing ring of Winkler-Waldeyer.

Describe ovular implantation and placentation.

When the ovum implants, it is an enlarging blastodermic vesicle surrounded by chorionic ectoderm. The encircling chorion is composed of two layers of cells, an outer layer of syncitiotrophoblasts or plasmotrophoblasts, and an inner layer of cytotrophoblasts or Langhans' cells. The trophoblasts erode the decidua and the embryo sinks into it and is contained within it. The opening in the decidua through which the egg entered is rapidly closed by deposition of fibrin and regeneration of decidual cells. The trophoblastic cover develops solid cellular buds about the twelfth day and these are the forerunners of the chorionic villi. Five or 6 days later, these buds receive a mesodermal core from the somatic mesoderm. Shortly thereafter, vascularization begins in the mesoderm. As the chorionic villi develop, some take root in the basal layer of the decidua (anchoring villi) and others erode into maternal vascular channels (nourishing villi). Villous development is most luxuriant beneath the ovum, which has now spread rapidly beneath the decidual surface. These villi beneath the ovum comprise the chorion frondosum, and it is from them that the placenta is formed. The other villi form the chorion laeve and are destined to atrophy. Meanwhile, the decidua, and particularly that beneath the ovum, becomes very vascular. The spiral arteries approach the placental site through the myometrium, lose all their coats save their endothelial linings, and empty directly into large vascular sinuses. Destruction of the decidua and vessel walls by the growing chorion produces these large vascular lakes or sinuses. The chorionic plate, the mass of chorion from which the placental villi take origin, forms the roof of these lakes and the endothelium of the decidual vessels, the floor and sides of them. The chorionic cells share the property of the endothelial cells of not interfering with the fluid nature of blood. The lakes drain through venous connections in their floor. The chorionic villi are bathed directly in these huge vascular spaces by maternal blood flowing through the intervillous spaces of the chorionic roof. The most peripheral blood lake of the placenta is called the "marginal sinus."

What are the functions of the placenta?

The placenta secretes hormones, accomplishes the selective exchange of substances between the fetal and maternal circulations, and acts as a barrier between the fetal and maternal circulations. The hormones that the placenta manufactures are chorionic gonadotropin, estrogen, and progesterone. The first of these is synthesized by the cytotrophoblasts and the latter two by the syncitiotrophoblasts. The exchange of substances between the two circulations is accomplished by the chorionic villi by rapid diffusion, slow diffusion, diffusion helped by enzymatic activity within the villi, and pinocytosis. Electrolytes, oxygen, carbon dioxide, and water, all substances required for fetal homeostasis, are thought to be transferred by the first process. Substances of large molecular composition, like the hormones, are thought to pass from one circulation to the other by a process of slow diffusion. Diffusion plus enzymatic activity accomplish the transfer of amino acids, sugars, and vitamins. Antibodies are an example of substances transferred by pinocytosis. The placenta acts as a barrier preventing the admixture of fetal and maternal blood as long as the villi remain functionally and physically intact. The chorionic trophoblastic layers, the jelly of Wharton, and the vascular wall of the fetal vessels lie between the fetal and maternal blood. Distinctive enzyme systems in the villi may play a role in the "barrier" function of the placenta. The villi may break off or be badly damaged by ischemia, circulating toxins, or senescence, and, as a result, lose their selectivity of transfer or even permit free admixture of the two circulations. Rh sensitization is an example of a failure of the placental barrier. Rh positive cells from the fetus enter the Rh negative blood of the mother and stimulate antibody formation by the maternal organism.

Describe the placenta at term.

The average placenta at term is an irregular ovoid with a diameter of 15 to 20 cm. and a thickness of 1.5 to 3 cm. Its weight is about one fifth to one sixth that of the fetus or usually about 500 gm. The side of the placenta that was toward the myometrium is termed the maternal side, that toward the amniotic sac, the fetal side. When the placenta separates, the cleavage plane is through the spongy layer of the decidua. The maternal side is, therefore, shaggy, with a surface composed of the compacta and part of the spongiosa of the decidua basalis. The decidua is gray, but, since it is translucent, the dark-red chorionic tissue beneath it shines through, giving the maternal side a deep gray-red color. The large blood spaces that distended and lay within the decidua during its period of function are not evident because they are empty and collapsed.

The most peripheral of these blood spaces is the *marginal sinus*. It has special significance because it may be a source of bleeding (maternal), at or near term or during labor. The maternal side is divided into segments, called cotyledons, by septa of decidua. The color of the fetal side of the placenta is a blue-gray. This side is covered by the shiny amnion. The umbilical cord inserts into it, usually near its center. The branching umbilical vessels are visible beneath the amniotic cover. Occasionally, a small yellow body is evident beneath the amnion near the insertion of the cord along with a white cordlike structure that extends from the yellow body to the umbilical cord. These are the remains of the vitelline vesicle and duct. Surrounding the placenta on the fetal side and marking the peripheral attachment of the amnion is a raised ridge, the closing ring of Winkler-Waldeyer. The subamniotic ridge consists of degenerated chorion and decidua.

Describe the umbilical cord at term; mention and comment briefly on two important anomalies or complications.

The umbilical cord is a smooth, shiny, slippery, pliable tube extending from the fetal umbilicus to the placenta. It is encased in amnion, and the area of insertion into the placenta is usually central. The matrix or stroma of the cord is a primitive mesodermal tissue, the jelly of Wharton. This matrix supports and protects the two umbilical arteries, which are placed peripherally, and a large umbilical vein, which is located centrally. The average length of the cord is 50 cm. and the diameter, 1 cm. In the mid-proximal cord, one can occasionally identify the fibrous cord that represents the obliterated allantois. Distally and beneath the amnion, which covers the placenta near the insertion of the cord, one can frequently identify a small yellow body from which a white coarse thread extends to the cord and disappears beneath its amnion. These are the remnants of the vitelline vesicle and duct. The umbilical vessels remain in the cord under normal circumstances until the cord inserts into the placenta. Only after insertion do the vessels branch and rebranch beneath the chorion to supply each villus.

Occasionally, however, the umbilical vessels branch some distance from the insertion and fan out over the placenta, unprotected by the jelly of Wharton and supported only by the thin amnion. This anomaly is called a velamentous insertion of the cord. Since the flaring, stretched, and unprotected vessels may be easily torn, the condition presents the potential complication of hemorrhage from the fetal circulation. Should the placenta be so placed that these vessels extend across the internal cervical os, the condition is called "vasa praevia." Vasa praevia will inevitably produce bleeding either as the cervix prepares for labor or as it dilates during parturition. The laboratory can distinguish between adult and fetal blood cells (normoblasts, nucleated red blood cells) and proof that the vaginal bleeding is of fetal origin helps confirm the diagnosis if suspected. Since the placenta may be low lying when a vasa praevia exists, the mechanism of the bleeding may combine that of placenta praevia and of vasa praevia. Since the bleeding of vasa praevia is fetal in origin, evidences of disproportionate fetal distress in the presence of painless vaginal bleeding at or near term or accompanying unusual bleeding during labor should make one think of this complication. Delivery of a healthy infant is usually accomplished by a cesarean section, which is done in the interests of the fetus.

Other cord problems include those incident to prolapse and compression, either occult or overt; true knot in the cord causing vascular compression; short cord, which may be torn or occluded by stretching as the fetus descends into the pelvis; and the rare and usually unexplained cord hematoma.

What is the amnion and how does it develop? How does it take part in the development of the umbilical cord?

The amnion or amniotic membrane is the inner of two envelopes that will surround the fetus. The outer one is the chorion. The amnion encloses a cavity, the amniotic sac, which contains amniotic fluid (see later question). It furnishes the environment best suited for fetal growth and development and, at the same time, protects it from external trauma and the umbilical cord from external pressures that might cut off the fetal circulation. The amniotic cavity also serves as a reservoir for fetal secretions and excretions. In addition, the amniotic fluid may contribute in a small way to fetal nutrition. The amniotic cavity can be identified late in the second week of embryonal life. It appears as a cleft in the ectoderm of the inner cell mass on the side destined to develop the fetal back. It is surrounded by ectodermal cells, and these are the primitive amniotic cells. Recent evidence suggests that the amnion develops from the continuing cellular divisions of a single cell that is predetestined for this purpose in very early ovular life. The cells of the amnion secrete the original amniotic fluid. The fluid-filled amniotic sac expands rapidly and unfolds around the fetus. Ultimately the fetus floats freely within it, connected to the periphery only by the umbilical cord. Its expansion completely displaces and replaces the chorionic cavity or exocoelom. In so doing, the amnion comes into intimate contact with the chorion everywhere save at the insertion of the body stalk, which is the bridge of primitive mesoderm that links the fetal mass (the inner cell mass) to the encircling chorion. This occurs about the beginning of the third month of embryonal life. The amnion also surrounds the body stalk, which has been lengthening and thinning as the fetal mass has been displaced centrally within the cavities of the chorion and amnion. In encircling the elongated body stalk, the amnion compresses the atrophying vitelline structures against its side and against the placenta adjacent to its insertion. Meanwhile, a hollow, blind, vestigial tube, the allantois (see later question), has atrophied. Blood vessels, the future umbilical vessels, have developed in the stalk. All of these structures of and adjacent to the body stalk are compressed together and enclosed by the amnion; the resulting structure is the umbilical cord.

What is the origin of amniotic fluid and how is its volume controlled?

The amnion secretes its fluid during its early life. In the fourth month, however, fetal urine becomes an important addition to the amniotic fluid. Other fetal secretions, excretions, or transudates probably contribute. Another important component of amniotic fluid is added probably about the same time. This is a transudate through the fetal membranes from the maternal body fluids. There also appears to be a fetal transudate through the amnion of the umbilical cord. The fluid and the substances contained in it presumably cross the membranous fetal envelope or envelopes in both directions. The processes by which this occurs have not been clarified: apparently the exchanges are selective. It is estimated that 50 per cent of the water molecules in the amniotic fluid are exchanged, under normal circumstances, with water molecules of the maternal fluids in about 1½ hours. The control of the amount of amniotic fluid present at a given time is also poorly understood. All the processes that govern its formation and exchange must participate in the determination of volume in some complex way. Here transudation through the umbilical amnion and the presence of selective systems in the umbilical cord may be particularly important. Fetal drinking of amniotic fluid and fetal urinary output are obvious sources of volumetric fluctuations. It is interesting that complete renal agenesis is associated with little or no amniotic fluid. Certain congenital fetal defects preventing fetal deglutition usually are accompanied by polyhydramnion.

What are the physical characteristics of amniotic fluid?

The normal amount of amniotic fluid at term varies from 700 to 2,000 ml. Less than 700 ml. is termed "oligohydramnion," more than 2,000 ml., "polyhydramnion." The fluid is slightly alkaline and has a specific gravity between 1.006 and 1.015. It has a yellowish tinge and it would be clear were it not for particles of vernix caseosa that are dispersed throughout it. The vernix is composed of a mixture of desquamated epithelium, lanugo, and sebaceous material from the fetus and of cholesterids and glycerids from the cells of the amnion.

Trace the development and life of the vitelline system and allantois.

While the amnion is forming on the dorsal side of the inner cell mass, the vitelline vesicle or yolk sac is developing on the ventral side. It is of entodermal origin and is soon in possession of a mesodermal sheath, as well as of its entodermal coat. At first, the growth of the vesicle into the exocoelom outstrips that of the amniotic sac, but this relationship reverses. After a brief span of activity, the vesicle atrophies. It is a negligible structure by the end of the third month of pregnancy. Like the amnion, the vitelline vesicle is filled with fluid. The growing fetal mass (inner cell mass) lies, as it were, on its abdomen on the vesicle. The fetus moves to a more central position in the exocoelom as the two sacs enlarge and, as it does, the body stalk lengthens. The fetus also lengthens and, as it does, its two ends curve sharply ventrally and then medially. As a result the ends double back on themselves and grow toward one another. In doing this, they pinch off the vitelline vesicle adjacent to the fetal mass and invaginate it into the fetus. This forms the primitive intestine. The connection between the gut and the vesicle remains open and is lengthened as the body stalk lengthens to form a tube, the vitelline duct. The duct parallels the body stalk. Eventually it lies along the entire length of the stalk and the regressing vesicle lies against the peripheral chorion (the placenta) adjacent to the distal insertion of the stalk. Meanwhile, a vestigial structure, the allantois, projects from the hind gut into the body stalk as a blind pouch; it atrophies along with the vitelline structures. The earliest embryonal blood circulation develops in the walls of the vitelline vesicle. It spreads to the fetus and, later, connects with the fetoplacental circulation. Early nourishment is carried to the fetus from the yolk sac by this first circulatory system. It atrophies rapidly, however, when the fetoplacental circulation is established and is nonfunctioning by the end of the third month of pregnancy. Its function is largely hematopoietic during its later days.

Describe the maternal-placental circulation.

Arterial blood enters the subplacental area, the basal layer of decidua, through the spiral uterine arteries. These lose their coats as they approach the placental area and open directly and without obstruction into the placental blood lakes through openings in the floor of these spaces. The relatively high arterial pressure spurts the fresh blood to the upper part of the spaces into which the chorionic villi dangle. The fresh maternal blood slows as it strikes the villi and then the interchange of substances between the fetal and maternal blood occurs. Such factors as the fetal blood flow coursing in the opposite direction from the maternal blood current, the higher oxygen content of the maternal blood compared with the fetal blood, and the unique carbon dioxide dissociation curve of the fetal blood add to the efficiency of the transfer. The slowed maternal blood settles toward the sinus floor where the venous openings gape to receive it. The low pressure in the veins compared with that of the sinus also directs the venous current toward the venous openings. The uterine contractions encourage the emptying of the maternal lakes and, therefore, indirectly encourage a more rapid arterial input. Each contraction compresses the myometrial veins and, as a result, empties them into the general venous circulation and then occludes them temporarily. A normal contraction, however, does not prevent the continuation of arterial blood flow into the sinuses. As a result, the pressure in the maternal spaces is increased by a contraction and a large, empty, low pressure reservoir is developed in the venous system. When the contraction ends and the venous openings are re-established, there is, therefore, an increased pressure differential between the spaces and the veins, and the used blood rushes out. The maternal placental circulation is a low pressure arteriovenous shunt that handles a blood flow of 500 to 600 cc. per minute at term. It has been compared to and has a number of points in common with an arteriovenous aneurysm. Pathologically strong uterine contractions, like those that may be encountered when oxytocin is used injudiciously, occlude both the arterial and venous openings in the placental lakes. The result can be dangerous fetal hypoxia.

Describe the fetal blood circulation.

The vitelline blood circulatory system becomes apparent in the third week of embryonal life and the chorionic circulation, in the fourth. The systems intercommunicate. The vitelline system rapidly takes on a very secondary role, however, as the chorionic circulation develops. The vitelline system completely disappears near the end of the first trimester of pregnancy, and its latter day function is primarily hematopoietic. The fetoplacental circulation is in operation by the end of the fourth week of embryonal life and it is the important and essential system from then on. The chorionic vascular network connects with the fetal circulation through the umbilical vessels. Each villus has an afferent artery that connects with an efferent vein. Early in embryonal life two umbilical arteries carry blood to the chorionic circulation and two umbilical veins collect and carry the blood from the villi. The two veins fuse quite early, however, and form one large, centrally placed, umbilical vein. In the functioning fetoplacental circulation the arterial blood from the fetus arrives in the villus to unburden its waste products into the maternal circulation and to be renewed. It is under relatively high pressure, perhaps 80 mm. of Hg because it must drive the blood back through the fetal venous system. Both fetal arterial and venous pressures in the villi must be higher than the pressure in the maternal vascular spaces into which they dip, or else the villous vessels would be compressed to occlusion by the surrounding pressure, and the fetal circulation halted. At rest, the pressure in the maternal lakes is estimated as about 10 mm. of Hg, the same pressure as that of the amniotic fluid. When the pressure in the lakes and amniotic fluid rises as a result of a contraction, the pressure on the fetus rises an equal amount. In turn, the pressure in the fetal arteries and veins rises the same amount. As a result, the pressure in the chorionc vessels always remains above the pressure in the maternal sinuses. The renewed fetal blood in the chorionic villi returns to the fetus through the villous veins, which drain into the umbilical vein. The fetal venous pressure is estimated as about 20 mm. of Hg, or a bit higher. The umbilical vein enters the fetus through the fetal umbilicus and turns upward beneath the parietal peritoneum to the liver. From here the blood takes three routes to the right atrium of the heart: the hepatic vessels, the portal vessels, and the vena cava via the ductus venosus. The right atrium propels the blood into the right ventricle, which in turn pumps it into the pulmonary artery. The pulmonary circulation is minimal in intrauterine life and most of the blood in the pulmonary artery is shunted directly into the aorta through the connecting ductus arteriosus. The right atrial blood is sped to the aorta by the second route. Pressure is low in the left atrium because of the minimal blood flow through the fetal venous system. The right atrial blood flows rapidly, therefore, through the foramen ovali, an opening in the interatrial septum, into the left atrium. It is pumped from there into the left ventricle and thence into the aorta. The blood circulates through the fetal arterial system, supplying tissue requirements and accepting the waste products of metabolism. Having completed the circuit, it leaves the fetus through two large arteries, one of which branches from each hypogastric artery. These two arterial branches become the two umbilical arteries, which return the blood to the placenta and its villi. As soon as the infant is born and breathes, the rich pulmonary circulation is established. Blood no longer shunts through the ductus arteriosus but flows through the lungs. Returning from the lungs, it fills the left atrium. The increase in flow to the left atrium coupled with the reduction of blood flow to the right atrium, the result of the discontinuation of the umbilical circulation, equalizes atrial pressures. Blood is no longer shunted, therefore, through the foramen ovali. As a result, both the foramen ovali and ductus arteriosus close functionally shortly after birth. Physical closure usually occurs within a couple of months of birth. Disuse also leads to obliteration of the intrafetal portions of the umbilical arteries and vein. The ductus arteriosum becomes the ligamentum arteriosum; the umbilical vein, the ligamentum teres; the ductus venosus, the ligamentum venosum; and the umbilical arteries, the ligamentum hypogastricum.

How does pregnancy affect the maternal cardiovascular system?

The dynamics of the maternal cardiovascular system begin to change as a result of pregnancy between the middle and end of the first trimester. These changes gradually increase the cardiac load up to about the thirtieth week of pregnancy. Thereafter, continuing changes involving the same factors reduce the cardiac work as term approaches. Venous pressure increases in the dependent parts. The veins become distended with blood and the venous return to the heart is increased. In contrast, the blood pressure, and in particular, the diastolic pressure, decreases moderately. The pulse pressure, therefore, increases. These changes in arterial circulation reflect a general decrease in peripheral vascular resistance, a change due in great part to the development of the placental circulation. Meanwhile, blood volume increases; expansion of the plasma fraction is greater than that of the cellular elements. Blood flow increases generally but the increase is shared differently. The renal and uterine circulations are among those particularly augmented. Arteriovenous oxygen difference decreases as a result of the changing metabolic demands and the circulatory changes. Cardiac rate and stroke volume increase. The sum of these readjustments, which reflect hormonal and anatomical changes and increased maternal and fetal requirements, require the two most important changes, namely, an increase in cardiac output and an increase in cardiac work. The cardiac output increases 30 to 50 per cent. At its height, about the thirtieth week of pregnancy, the increase is in the range of 1,500 ml. per minute; at term, it has dropped to 800 ml.

How does early pregnancy affect the gastrointestinal tract; what is hyperemesis gravidarum and how is it treated?

The physiological symptoms of early pregnancy vary greatly in severity. They may be practically absent or consist only of gaseous eructation and distention, or mild indigestion. In contrast, nausea and vomiting may become quite severe. In general, the *symptoms* are limited to the first 12 or 14 weeks and their peak of severity is at about the ninth or tenth week. The symptoms and their severity parallel the activity of the chorionic cytotrophoblasts. Excretions of these cells or the end results of their activity are thought to be etiological in this condition. The symptoms are routinely aggravated by such things as tiredness, emotional disturbances, and intercurrent illness. An interesting subtype of this problem is ptyalism. In this instance the patient constantly has a mouthful of saliva and is continually drooling or spitting. This condition results from the inability of the patient to swallow, rather than to excessive production of saliva. Strong suggestive therapy (hypnosis) is the best treatment for this particular complication.

The *therapeutic regimen* for hyperemesis consists of reassurance, rest, and mild sedation. Frequent small feedings, often of dry and salty food, are helpful. Fluid intake is similarly spaced and limited. Frequently, ice-cold carbonated drinks can be retained with the least trouble. Pyridoxine in adequate dosage (100 to 200 mg. per day) prescribed alone or with one of the tranquilizing antihistaminic type of drugs is as promising as any specific therapy. Also, in these cases, suggestion is a very helpful tool. *Hyperemesis gravidarum* is a pathological degree of the "physiological" hyperemesis of early pregnancy. It must be distinguished by study and history from organic gastrointestinal problems that are aggravated by pregnancy. Hyperemesis is usually, and perhaps almost always, a functional or psychophysiological disease. The psychic background of it may be superficial and relatively amenable to therapy or extremely complex and deeply rooted in the subconscious. It can develop on a background of a chronically, hyperreacting, functional gastrointestinal illness. An individual sensitivity or allergy to chorionic gonadotropin or an end product of its activity, has been indicted as etiological in some cases. Nausea and vomiting are severe and constant. Fluid and electrolyte imbalance, starvation, and the results of starvation are inevitable complications or are parts of the illness. Continuation of the process, usually untreated or inadequately treated, may lead to hepatic, renal, and/or cardiovascular failure. Polyneuritis and dementia may develop. Death may occur with irreversible tissue changes in a number of essential organs, the development of coma, and finally, cardiovascular failure. Severe fatal hyperemesis is a rarity where modern obstetrics is practiced. When the gastrointestinal symptoms become moderately severe, the patient is hospitalized and therapy instituted. This is similar to but more aggressive than that used in the therapy of the milder gastrointestinal problems. Food may be withheld for a few days and alimentation and hydration accomplished by the intravenous route. Occasionally a stomach tube is used for the same purpose. With the help of laboratory and vital bedside data, including routine recordings plus measurement of intake and output, fluid and electrolyte balance are regained and maintained. Calories, vitamins, et al. are provided parenterally. Attention is given to the patient's comfort and psychological needs. With improvement, oral feedings are cautiously started and increased. Thus, the onset of serious and irreversible complications seems impossible when therapy is active and carefully planned and controlled. Some patients, however, apparently do not respond; corticosteroids are said to be helpful in these more difficult cases. Any and all general supportive measures are employed. Rarely, pregnancy must be terminated. This is done only if the disease is progressive despite adequate medical care. This radical approach is today a true rarity. If the disease has progressed to a point of severe and irreparable damage to vital organs, nothing will save the patient.

Discuss changes in the metabolism of protein, carbohydrates, and fat that occur during pregnancy in the maternal organism.

Protein: Nitrogen is conserved and retained by the maternal organism for: (*a*) growth of the fetus, placenta, and maternal organism; (*b*) increased requirements for tissue regeneration that result from the increased physical burden of pregnancy and alterations in thyroid function and carbohydrate metabolism; (*c*) for maintenance and increase of the body surplus.

Carbohydrates: (*a*) The renal threshold for carbohydrate is lowered; (*b*) there is a decrease in carbohydrate tolerance, probably the result of a change in pituitary activity and possibly contributed to by a reduction in the ability of the liver to store sugar; (*c*) the blood sugar is slightly lowered. Despite this, however, intermittent glycosuria may appear as the result of (*a*) and (*b*). A positive test for sugar in the urine may also result near term from lactose that is present in the blood in increased amount.

Fat: The fatty elements in the blood increase as a result of an increase in absorption of fat from the intestinal tract.

Discuss the differential diagnoses of early pregnancy.

The diagnosis of pregnancy must be considered in the case of any patient of childbearing age who gives a history of menstrual irregularity—particularly, of the sudden onset of amenorrhea—or exhibits general or pelvic findings that include any of the suggestive signs of early pregnancy, especially that of uterine enlargement. History may give the best lead to the correct diagnosis in very early pregnancy. A careful history of sexual contact and contraceptive habits is helpful. One must remember, however, that a patient may forget important information and may, on occasion, be hesitant to report the truth, or may even want to mislead the physician by what she tells him.

Once pregnancy is under consideration, he tries to elicit a history of symptoms suggestive of pregnancy other than that of the suggestive menstrual change. The symptoms of pregnancy are easily copied or produced, however, by suggestion. This is particularly true in the patient who is overly avid to conceive or terribly frightened of conceiving. These two groups form the largest number with cases of pseudocyesis, or false pregnancy. In this unusual condition, the patient develops the symptoms of pregnancy and many of the signs as a result of a functional disturbance. The history must include a general survey, with emphasis on situations other than pregnancy that might account for the patient's symptom complex. A history of previous and possibly similar episodes is sought.

A history of the patient's general health is also obtained. Chronic illness and occasionally acute intercurrent disease may alter the menstrual pattern and provoke symptoms encountered in pregnancy. In the physically healthy girl, emotional pressures, tensions, and conflicts are a frequent—and in the case of the nonpregnant—most frequent cause of menstrual changes and other vague symptoms of a type that might accompany pregnancy. An iatrogenic pseudocyesis can be suspected from the history. Uninterrupted ovarian hormone therapy may produce prolonged amenorrhea, as well as other signs and symptoms suggestive of pregnancy.

The presence of an enlarged pelvic mass, particularly if it is soft and tends to be in the midline, should always suggest pregnancy. An intact hymen does not rule out the possibility. The mass may confuse diagnosis in one of two ways: it may hide a pregnancy; it may falsely suggest a pregnancy. The mass may be uterine or adnexal. Uterine enlargement may be due to a number of conditions: hypertrophic enlargement that has resulted from previous pregnancies and subinvolution; fibromyomas; adenomyosis; the congestion incident to a retroversion or even a delayed menstrual period; and the retention of fluids within the uterus. The most common cause of this latter condition is cervical stenosis that has resulted from conization or cauterization of the cervix. The retained material is usually blood (hematometra). Periodic, severe, labor-like cramps in a patient with amenorrhea and a history of cervical surgery suggest the correct diagnosis. Too, the cervical stenosis may be very evident from the examination.

Adnexal pathology may also make diagnosis difficult. A cystic adnexal lesion adherent to the uterus may suggest uterine enlargement and softening and produce menstrual changes. Postinflammatory disease and endometriosis are examples of this type of situation. The patient's history is often helpful in making the correct diagnosis. An ovarian cyst may be mistaken for a cystically enlarged uterus or hide one. When a cystic adnexal lesion is combined with suspicious signs and symptoms of pregnancy, the possibility of an ectopic pregnancy must be inserted as a possibility. On the other hand, the palpable ovarian enlargement could be the corpus luteum of pregnancy. Usually, nonpregnant uterine enlargements are firmer than those of the pregnant uteri and cystic adnexal enlargements are softer. Too, the latter are often more lobulated than a pregnant uterus and may be either more freely movable, or more fixed, than the usual gravid uterus. Lateral displacement of adnexal tumors and the ability to separate them from the uterus are additional signs of differential value. Problems interfering with a good pelvic examination increase the difficulty of diagnosis. Improper positioning of the patient for examination and a poor light source are among the causes of error. A full bladder or bowel may interfere seriously with accurate bimanual examination. The obesity of a patient or her inability to relax pose additional problems. Abdominal distention from gas or ascites may also confuse the issue.

Pregnancy tests are extremely valuable in making the correct diagnosis and should be used if early diagnosis is important. These tests must be used, however, with knowledge of their limitations. A suggestive history plus suggestive signs usually place the diagnosis of pregnancy into the category of the "probably correct." Serial pelvic examinations however, are very valuable in certifying the diagnosis of pregnancy. When repeated examinations show a relatively rapidly enlarging, doughy pelvic mass that preferably is associated with other suggestive signs and symptoms of pregnancy, possibly including a positive biological test, the diagnosis of pregnancy is as certain as is possible before the so-called "certain" signs of pregnancy appear in the second trimester. One should remember that symptoms and uterine signs of pregnancy may be present but unusually mild in the presence of a "blighted ova" pregnancy destined for abortion or of an ectopic pregnancy.

Name and briefly describe the common tests used for the diagnosis of pregnancy.

The biological tests for pregnancy are based on the presence of chorionic gonadotropin in the blood, serum, and urine of pregnant women. The concentration of this hormone is sufficiently high in each type of specimen to make each test 95 per cent accurate on samples taken two weeks or more beyond the missed period. These tests may even be positive within the week after the missed period but accuracy decreases with the shortened interval. A given amount of the specimen is injected by one route or another into an appropriate test animal for the given test, and a designated end point is evaluated after a specific time interval from injection. The four most commonly used biological tests and their end points are: (1) *Aschheim-Zondek* *test:* maturation of the ovaries of immature mice as evidenced by the presence of hemorrhagic follicles or corpora lutea; (2) *Friedman test:* evidence of ovulation in the ovaries of healthy, young, mature rabbits that have been isolated from the male for at least three weeks; (3) *male frog and toad test:* ejaculation of spermatozoa by the male frog. False positive reactions are significantly increased among patients taking tranquilizers; Promazine and chlorpromazine have been indicted. Most of the false reactions seem to be eliminated by using maternal serum for the test. The incidence of false positives can also be reduced by the addition of certain technical steps; (4) *ovarian hyperemia test:* development of a red appearance of the ovaries of immature rats. The color, due to hyperemia, is evaluated by comparison with a standard color chart. *Basal temperature determinations* may be used to diagnose pregnancy with accuracy equal to that of the biological tests. Normally, the basal temperature rises at the time of ovulation and returns to normal at the end of the average menstrual cycle. In the presence of pregnancy, the temperature elevation continues beyond the calculated date of menstruation. The temperature rise is due to progesterone.

Distinguish between parity and gravidity.

The term "gravid" refers to a pregnancy, per se, irrespective of outcome. Thus, abortions, ectopics, and an existent undelivered pregnancy count in gravidity. A multiple pregnancy adds only one in the calculations. The pregnant patient is a gravida; when in labor, a parturient; and after delivery, a parous woman. Parity refers to a pregnancy that has resulted in the delivery of a potentially viable infant or infants, whether dead or alive, and irrespective of method of delivery. "Nulliparous," "primiparous," and "multiparous" refer to individuals who have delivered no children, one child, and two or more children respectively.

How is the expected date of confinement for pregnancy calculated?

There is no accurate way by which to determine in advance the date on which spontaneous labor will occur. This is true even when exact dates of menstruation, fertilization, and important events of pregnancy are known. The best date from which to predict is the date of fertile intercourse or insemination. With this as a guide, data of different investigators indicate that the average duration of pregnancy from fertile contact is almost any span of days from 265 to 273. Each is willing to subtract or add 5 to 14 days to include the normal span. When there is a past history of successful pregnancy, one may feel reasonably safe in predicting that the duration of a present pregnancy will be close to that or those of the past. A given couple seems to have their individual number of days of pregnancy to reach their individual "term." This is not as valid, however, if the previous labor followed rupture of the membranes. The latter often seems to be a happenstance that can occur any time as term approaches.

Some of the systems or methods by which the expected date of confinement and/or the maturity of pregnancy can be estimated with some accuracy are, briefly: (1) *Naegele's Rule:* Term is 280 days after the first day of the last menstrual period, assuming a 28 day cycle, or 265 days after conception. The former computation is accomplished rapidly by subtracting 3 months from the date of the first day of the last normal period and adding 7 days. Correction is made for the shifted time of ovulation if the cycles are not 28 days. Theoretically, the day of ovulation is the total number of days of the cycle minus 14. (2) This gives the *expected month of confinement*—the day of the month will be the same as the day of the month on which conception occurred or will span the dates of probable fertilization, as determined by the theoretical dates of ovulation (see 1 above). (3) *Quickening* occurs at about 16 weeks in a woman who has previously experienced fetal activity and at 18 weeks in the uninitiated. Term is considered as 40 weeks. (4) *Certain objective measurements* or observations may be used as a starting point for calculations: These are bound to be inaccurate approximations because they are based on measurements of the uterus or its fetus, for estimates of fetal size and basic data include a wide span of normals. Furthermore, the accuracy of these measurements will vary according to such unpredictable variables as the thickness of the abdominal wall and the amount of amniotic fluid surrounding the fetus. Palpatory estimation of fetal size is notoriously inaccurate, although accuracy improves with practice. The other important variable that is introduced if these data are used to estimate duration of pregnancy arises from the fact that the fetal weight, length, and other measurements of a given fetus may vary greatly from the average data recorded for a typical fetus of the same age. Nonetheless, each measurement or estimation adds one more bit of evidence and at times this is needed. The height of the fundus above the symphysis, the length of the arc of the external surface of the abdominal wall from symphysis to fundus, and the occipitofrontal diameter of the fetal head, measured through the lower abdominal wall, are some of the more helpful measurements. Roentgenographic estimates of fetal age, based on measurements and development of centers of ossification are also unreliable because of individual fetal variations.

Vaginal and abdominal examinations as term approaches may prove very helpful in predicting labor. The presenting part drops into the true pelvis, according to didactic teaching, 3 weeks prior to delivery. This phenomenon, *"lightening,"* occurs, in fact, in variable relationship to labor. *"Ripening"* of the cervix—that is, effacement, dilatation, and the development of elasticity of the cervix—is one of the best signs that labor is not far off.

List the common symptoms of early pregnancy.

(1) Establishment of amenorrhea in a healthy woman of childbearing age without apparent cause other than pregnancy; occasionally, the substitution of scant vaginal bleeding for the usual menstrual flow at the time of or near the expected date of menstruation (the "sting of the egg," or "implantation sign"). (2) Pelvic symptoms suggestive of menstruation, particularly menstrual-like cramps, occurring at the time of the missed period and continuing for a time thereafter; occasional pain in the right or left lower quadrant of the abdomen, often stimulated by change in position. (3) Aggravation of the usual premenstrual symptoms prior to the missed period and continuation of them beyond the expected date of menstruation. (4) Unusual and unaccountable tiredness or lassitude; change in mood and emotionalism. (5) Increase in breast size and sensitivity; tenderness and reactivity of the nipples. (6) Increase in pigmentation, particularly of the nipples and breast areola; hypertrophy of Montgomery's follicles. (7) Gastrointestinal symptoms of variable severity; indigestion, flatulence, gaseous abdominal distention, nausea, vomiting, change in bowel habits, ptyalism. (8) Urinary frequency. (9) Vascular prominence, particularly of the veins of the breasts, legs, and vulva.

List the pelvic signs of early pregnancy.

(1) Cyanosis of the cervix and, to a lesser degree, of the vaginal and vulvar skins (*Chadwick's sign*); (2) vulvo vaginal-cervical softening (*Goodell's sign*); (3) softening of the lower uterine segment (*Hegar's sign*); (4) compressibility of the lower uterine segment; (5) uterine contractility detectable by the examining fingers during bimanual examination (*Hicks's sign*); (6) uterine growth (size and weight) and change in con-

tour; (7) alteration in uterine axis and mobility.

Distinguish between the "presumptive-probable" and the "certain" signs and symptoms of pregnancy.

The signs and symptoms of pregnancy that are listed in the questions immediately preceding this one are all *presumptive and probable*. One could add to these lists "quickening" or the subjective feeling of fetal movements (16 to 18 weeks), a positive biological test for pregnancy, and auscultation of a uterine souffle. The *certain signs* are not apparent until the second trimester of pregnancy. They are: objective palpation of a fetus and/or fetal movements, ballottement of a fetus, audible fetal heart sounds or funic souffle, fetal heart beat distinguishable by electrocardiography, aspiration of amniotic fluid from the uterine cavity, roentgenographic demonstration of a fetus, and serial findings showing progressive changes in uterine size, shape, and position, compatible with those expected with a normally developing pregnancy.

Define "presentation," "lie," "presenting part," and "attitude."

Presentation, or *lie,* is the relationship of the long axis of the fetus to the long axis of the mother. It can be longitudinal, transverse, or oblique. Presentation can also be substituted as a synonym for *presenting part*. Used in this way, it refers to the fetal part that is lowest in the maternal pelvis, or that part encountered first when the examining finger is inserted through the cervix. Thus, a longitudinal presentation is also either a cephalic or breech presentation. *Attitude* is the relationship of the fetal parts to one another. There are two attitudes: flexion and extension.

Evaluate the factors influencing fetal presentation, position, and attitude.

The fetus in its normal flexion attitude simulates two ovoids (the head and breech) connected by a straight axis (the spine). The uterine cavity at term can also be translated into two ovoids (the lower segment and the corpus) lying one above the other and connected by a longitudinal axis. According to the physical laws of accommodation, the fetus fits into the uterine cavity best when the cephalic ovoid lies in the lower segment and the presentation is longitudinal. This thesis, which accounts for the most common fetal presentation, is called the "accommodation theory." The "accommodation" of the fetus to the uterine cavity is aided by uterine contractility, fetal movements, and gravity. At term the specific gravity of the fetal head is greater than that of the breech.

The normal dextrorotation of the uterus and the indentation of the left, lower, posterior segment of the uterus by the sigmoid tend to rotate the presenting part clockwise. As a result, the most frequent position of the cephalic presentation is L.O.A. Other factors, however, play roles of varying and individual importance in the determination of presentations, positions, and attitudes. In early and mid-pregnancy, the uterus and its cavity tend to be spheroid and, therefore, lack polarity. Furthermore, the intrauterine volume in which the fetus is contained is relatively great as compared to fetal size. This spatial relationship is continued or redeveloped in cases of polyhydramnion. In these situations, the fetus can move about freely and presentation is not influenced appreciably by the laws of accommodation. A somewhat similar situation is still present physiologically in the early part of the last trimester of pregnancy. Only toward the mid-portion of the last trimester does a decrease in amniotic fluid, a rapid increase in fetal size, and an increase in uterine contractility and tonus structure provide the physical environment which the laws of accommodation dictate for a longitudinal lie and favor a cephalic presentation. At this time, it becomes difficult, if not impossible, for the fetus to reverse poles. It can, however, continue to rotate on its long axis. Rotation of the fetus on its long axis is usually prevented as term approaches by the presenting part engaging, or at least dipping into, the pelvic inlet. Anything interfering with engagement or accommodation to the pelvic inlet permits freedom of movement of the presenting part. In this circumstance, flexion or extension of the head may offer some cephalic diameter that does fit into the pelvic inlet. When this occurs, the head is anchored in what may be an unusual attitude.

It is evident that chance plays the all-important role in determining presentation, position, and attitude in some cases. An illustration of this is evident in the case of the frank breech. In this example, it is presumed that the fetus happened by chance to be presenting as a breech when spatial changes interfered with a further change in polarity. In attempting to move, both legs were caught in the extended position and, thereafter, could not be flexed. This latter development certified the breech position because the extended legs splinted the body and spine. Body flexion that would be essential for a change in polarity could no longer be accomplished. The factors that produce malpresentations in such situations, as prematurity, polyhydramnion, cephalopelvic disproportion, and hydrocephalus, are evident from the above analyses. Other conditions that may influence the development of unusual presentations or positions include: loss of myometrial tone, usually the result of multiparity; relaxed abdominal and pelvic supports permitting displacement of both the normal uterine axis and the fetal axis; pelvic tumors, particularly submucus, uterine tumors; placental position; fixation of the umbilical cord around a fetal extremity; and fetal tumors, for example, an enlarged thyroid, which would cause extension of the fetal head.

What are labor, eutocia, and dystocia?

Labor is the involuntary activity of the uterus, supplemented usually by the voluntary expulsive powers of the parturient, frequently aided by the skills of an obstetrician, by which the viable products of conception are delivered or an attempt is made at their delivery, from the gravid uterus through the vagina. *Eutocia* is normal labor. *Dystocia* is abnormal labor.

What are the essential factors influencing labor?

The Powers of Expulsion: Involuntary contractions of the uterus and its supporting ligaments; voluntary contractions of the abdominal muscles.

The Passages: The bony pelvis and its fibromuscular soft tissues.

The Passengers: The fetus and placenta.

Describe the true bony pelvis.

The true or obstetrical pelvis lies between the superior strait or plane of the pelvic inlet and the inferior strait or plane of the outlet. The former is heart-shaped and is bounded by the promontory of the sacrum posteriorly, the linea terminalis of the innominate bones laterally, and the superior border of the pubis anteriorly. The anteroposterior diameter of the inlet in the erect patient inclines upward at an angle of 55 degrees from a line to the horizon. The similar angle of the plane of the outlet is only 10 degrees. The widest diameter, a transverse, crossing the pelvis 4.5 cm. in front of the sacrum, measures 13 cm. The anteroposterior diameter of the inlet is 11.5 cm. An anteroposterior diameter to a point about 1 cm. lower on the sacrum is a more important measurement. It extends from the superior border of the symphysis to an imaginary extension of the iliopectineal lines on the first sacral segment. Called the obstetrical conjugate, it is the shortest anteroposterior diameter traversed by the fetus, and it measures 11.0 cm. The oblique diameters extend from the sacroiliac joint on the designated side to the iliopectineal tubercle of the opposite side. The right oblique of the inlet is 12.5 cm. and the left, 12.0 cm. The plane of the outlet is a quadrilateral. It is bounded by the tip of the coccyx posteriorly, the ischial tuberosities laterally, and the lower edge of the symphysis pubis anteriorly. Since the tuberosities are lower than the anterior and posterior landmarks, the outlet may be thought of as two triangular inclined planes with an identical base—a line joining the tuberosities. The perpendicular of the posterior triangle is the posterior sagittal diameter, which measures 9 cm. The anterior sagittal diameter is 6 cm. The diameter from the symphysis to the coccyx is 9.5 cm., but it is increased to 11.5 cm. as the descending presenting part displaces the coccyx posteriorly. The transverse of the outlet is 10.5 cm. The pelvic excavation is the anteriorly curved cylindrical passage between the superior and inferior straits. Two of its planes are worthy of note. The widest pelvic plane is an irregular ovoid that lies at right angles to the cylindrical passage and extends from mid-point of the posterior pubic surface to the junction of the second and third sacral vertebrae. Its anteroposterior measurement is 13.5 cm. and its transverse, 12.5 cm. The narrowest pelvic plane is lower in the pelvis and at that level where the cylindrical passage curves anteriorly. It is bounded by the lower border of the sacrum posteriorly, the ischial spines laterally, and the inferior border of the pubic arch anteriorly. The anteroposterior diameter is 11.5 cm. and the interspinous diameter is 11.0 cm. The posterior sagittal diameter, the distance from the interspinous diameter to the sacrococcygeal joint, is 5 cm. The depth of the birth canal anteriorly is the width of the symphysis pubis, which averages 4.5 cm.; the depth posteriorly is the height of the sacrum, 12.5 cm.

What are the fascial and muscular structures of the pelvis that are of obstetric significance; how are they affected by labor; how do they affect labor?

The psoas, pyriformis, and obturator internus muscles and their fascias "line" the birth canal. They decrease the pelvic diameters insignificantly and, therefore, have little effect on and are but little affected by the passage of the fetus through the pelvis. On the other hand, the pelvic floor or diaphragm and the urogenital diaphragm through which the fetus passes on its way to the outside play important roles in the mechanism of labor and may be seriously damaged by the passage of the fetus or attempts to aid in its delivery.

The *levator ani muscle* and *fascia* comprise the *pelvic diaphragm.* A slinglike structure, it forms a trough from planes on both sides inclined downward and inward. These guide the descending presenting part anteriorly and cause it to rotate. The pressure of the descending part, which may be pathologically increased by the pull of obstetrical forceps, stretches the muscle downward, backward, and centrifugally. Even in the absence of gross lacerations, vaginal delivery weakens the pelvic floor. Lacerations may occur, particularly posterolaterally on either side of the posterior vaginal wall, as a so-called sulcus tear.

Below the levator ani muscle and fascia and, therefore, more superficially located, are other supporting muscles through which the vagina extends. In the forward part toward the symphysis, the so-called anterior triangle, is the *urogenital diaphragm* and, superficial to it, the bulbo- and ischiocavernosus and the superficial transverse perineal muscle. The anal sphincter is the important muscle of the posterior triangle. The urogenital diaphragm is contained between a superior and inferior fascia and includes the deep transverse perineal muscle and the compressor urethrae. Between the vagina and rectum, they form the muscular tissue of the perineum. These muscles also take part in guiding and rotating the presenting part now approaching delivery. The pressure on them is centrifugal and downward as the presenting part distends the perineum and the vaginal introitus. Episiotomy is designed to prevent harmful overdistention or laceration of these muscles. Should a perineal laceration extend posteriorly to sever the anal sphincter, fecal incontinence would result unless the injury were diagnosed and repaired.

The *endopelvic fascia* is the other important soft tissue involved in vaginal delivery. It surrounds the cervix and fans out to the pelvic walls in condensations named the cardinal ligaments (the base of the broad ligaments), uterosacral ligaments, and the pubocervical (anterior vaginal wall) and rectovaginal (posterior vaginal wall) fascias (here the word fascia is probably a misnomer). The first three of these structures are the primary uterine supports, holding the uterus upward as the passage is forced downward and out. Having little elasticity, these structures and particularly those of the vaginal walls, which must stretch sufficiently to permit passage of the fetus, are inevitably weakened permanently to some extent. Significant lacerations of them, or too great or oft repeated stretchings, are the background for subsequent uterine malposition or prolapse and for cystoceles and rectoceles.

Describe the head of an average newborn, giving the names and average values of the important diameters and circumferences.

The cranium, which, with the face and base of the skull, comprise the fetal or newborn head, is the important obstetrical entity of the head. It is made up of 7 thin, malleable bones that are united by membranous joints called "sutures." The 7 bones are the occipital, and the paired frontal, parietal, and temporal bones. The sagittal, coronal or parietal, and the lambdoidal sutures unite the parietal, frontal and parietal, and occipital and parietal bones respectively. The frontal, sagittal, and parietal sutures intersect in a diamond-shaped fossa, the large anterior fontanel, also called the bregma. The lambdoidal and sagittal sutures converge to form a Y in the small, posterior fontanel. The synciput is the area in front of the bregma; the vertex, the area between the two fontanels; and the occiput, the area posterior to the Y-shaped fontanel. The occipitofrontal circumference of the infant head at term is 34 cm., and the suboccipitobregmatic diameter, 31 cm. The longest diameter of the fetal head, the occipitomental diameter (the diameter of the extended head), is 13 cm.; the shortest, the suboccipitobregmatic diameter (that of flexion), is 9.5 cm.; the direct A.P. diameter, the occipitofrontal (the head looking straight ahead), is 11 cm. The biparietal, or widest diameter, is 9.5 cm.

Define and classify labor.

Labor is the maternal process by which a product of conception of viable development is expelled from the uterus through the vagina to the outside. The diagnostic criteria for viability vary from state to state and clinic to clinic. The expulsion and delivery of the products of a previable conceptus is abortion. Labor may be classified as normal or abnormal. The former is eutocia, the latter, dystocia. The criteria by which one separates the abnormal from the normal are individual and variable.

Labor may also be classified according to the maturity of the pregnancy in relationship to estimated term. Term labor usually includes those deliveries between the beginning of the thirty-seventh and the end of the forty-fourth week of pregnancy. Premature labors develop before the thirty-seventh week. As generally used, the term "premature labor" refers specifically to the interval between the twenty-sixth or twenty-eighth week and the thirty-seventh week of pregnancy. "Premature labor" is also used to describe terminations between fetal viability and the twenty-sixth or twenty-eighth week. This latter group, however, is often distinguished in hospital coding by an additional restricting adjective or descriptive phrase of local significance, such as, "premature labor," "immature birth."

Describe the fetal heart sounds.

The heart sounds of the fetus are first heard, at about the eighteenth week of pregnancy, through the lower abdomen in the midline just above the pubis. Normally regular and rapid (120 to 160), they sound like the ticking of a watch beneath a pillow. As the fetus grows, they are heard best over the anterior fetal shoulder. A significant increase or, more importantly, decrease in rate suggests fetal distress.

Comment on the factors initiating labor.

In attempting to discover the factors that lead to these developments and, ultimately, to labor, one can only record certain changes that are known to occur during the final 3 months of normal pregnancies and then to synthesize from these observations some theory to account for the initiation of labor. One cannot know which of the factors or processes observed are causes and which effects, and which are more important and which less. It is equally impossible to certify the order in which the processes develop and act. Indeed, it is likely that the relationship of the factors, one to another, varies from case to case.

Among the observable changes that precede labor are the following: The amounts of circulating estrogens and progesterone increase almost to term and then drop off shortly before the onset of labor. The estrogen increases myometrial contractility but, at the same time, it is a defense against the contractility stimulated by uterine distention. Progesterone prevents important uterine contractions not through inactivation of the actomyosin-adenosine triphosphate system but rather by altering the membrane potential of the muscle fibers. Redistribution of cellular potassium is important in this change. The alteration in membrane potential permits frequent weak contractions of the myometrium but prevents strong, labor-like contractions. Intrauterine pressure and uterine distention, as well as alterations in these physical factors, are important in the over-all synthesis of factors leading to labor. The intrauterine volume changes, the amniotic fluid decreases, and the fetus grows more rapidly and loses water, which increases its specific gravity and causes it to press down against the cervix and lower uterine segment. Intramural tension decreases, probably as a result of blood-volume, vascular, and placental changes. Uterine growth relatively stops as a result of these changes. The lower uterine segment unfolds, permitting "lightening," the descent of the presenting part into the pelvis. This is due to contractions and permanent shortening of the fundal-corporeal myometrium and stretching of the lower uterine segment. The segment is stretched with relative ease because of its sparse musculature, low content of actomyosin, and patchy distribution of hypertrophic elastic tissue when compared with these substances in the thicker corpus and fundus. The cervix effaces and dilates as its vertically oriented, peripheral musculature pulls upward and the water-ladened, central mass of fibrous tissue and collagen gives way.

One can interrelate these changes in differently structured theories. In any event, it seems likely that the factors just summarized, and others, produce changes in the placenta—a physiological aging of the organ—that decrease the production of estrogen and, more importantly, progesterone and withdraw them from the circulation. In turn, these withdrawals release the potentially powerful contractility of the fundal-corporeal myometrium—a potential power that has been systematically augmented throughout pregnancy—and labor begins. That progressive placental senescence per se is not the whole story is indicated, however, by those cases that show definite signs of rather long-standing placental aging but that do not fall into labor for some time after degenerative changes are established. Although the development of labor is almost certainly a locally governed uteroplacental function, the abnormal labors associated with cases of tension that produce autonomic nervous system imbalance show that matters of general physiology have an important bearing on established labor and, one might infer from this, on the initiation of labor.

What are the criteria for induction of labor?

Most induced labors are done electively for the convenience of the patient or obstetrician or both. This "convenience" may, however, frequently provide definite physical and psychic advantages to the patient. Other labors are induced for medical and obstetrical reasons. One must adhere carefully to certain criteria in cases of elective induction. Although ideal, these criteria cannot always be so carefully followed for indicated inductions. As a rule, however, it is better to terminate a pregnancy, when termination is indicated, by elective cesarean section than to stray too far from the accepted criteria for induction with the hope of gaining vaginal delivery. First, there must be no urgency for delivery. Only cesarean section can guarantee prompt termination. Furthermore, in indicated terminations, one must estimate and compare all of the advantages of the vaginal versus the abdominal route. Assuming that the fetus is alive, its maturity must be guaranteed in elective induction and seriously considered when termination may be indicated. In elective inductions the obstetrical situation should be ideal; for example, there should be no question of cephalopelvic disproportion. The case for induction is usually predicted best by the condition of the cervix. The cervix should be "ripe": well effaced, dilated (preferably at least 2 cm.), elastic, and pliable. Some obstetricians require that the presenting part is the head. The presenting part should ideally be engaged or easily engageable. The uterus should be irritable. One can test and predict the responsiveness of the uterine muscle by giving measured small doses of oxytocin and observing the promptness and strength of the resulting contractions.

What are the dangers of induced labor?

The fetus may be endangered by: (1) intrauterine hypoxia incident to uterine spasm or a tumultuous labor resulting from oxytocin; (2) prolapse of the cord incident to rupture of the membranes (breech, high presenting part); (3) prematurity resulting from incorrect evaluation of the duration of pregnancy. The maternal dangers are incident to the development of either an abnormally active labor, the result of oxytocin stimulation, or to a labor complicated by inertia, the result of hyperreactivity of the uterus or an unripe cervix that is difficult to dilate. The former may cause uterine rupture (particularly in grand multipara), or cervical or lower genital-tract lacerations, followed by hemorrhage and shock. The latter might cause the problems inherent in prolonged labor and might require cesarean section or other operative obstetrical procedures for delivery.

What is the caput succedaneum?

After the membranes have ruptured, each uterine contraction presses the circumference of the leading part of the fetal head directly against the dilating cervix. The central portion of the presentation overlying the circular area of cervical dilatation is free of direct pressure. As a result, the soft tissues of this central area become congested, edematous, and the site of multiple foci of minor bleeding that originate from small ruptured blood vessels. The involved tissues swell and this swelling is the caput succedaneum. Its location is characteristic for each cephalic position.

What is the funic souffle? The placental souffle?

The funic souffle is the sound made by the fetal blood flowing through the umbilical vessels. It is a soft to-and-fro murmur that is louder in systole than diastole and is synchronous with the fetal heart beat. The placental souffle is the sound produced by the maternal blood rushing through the uterine vessels, which have been greatly enlarged by pregnancy. It is a loud to-and-fro murmur, heard more prominently in systole than diastole. It may be heard earlier than the fetal heart sounds and is synchronous with the maternal pulse. Since its origin requires only rapid blood flow through large pelvic vessels, it is of most significance in a negative way. It is neither indicative of pregnancy, placental location, nor fetal viability. In the presence of other signs or symptoms of pregnancy, it adds one more piece of suggestive evidence.

What is the mechanism of cervical dilatation and effacement?

The cervix and lower uterine segment are effaced and then dilated by the myometrial contractions of the corpus and fundus, termed the "contractile portion of the uterus." As contractions shorten the myometrial fibers, pull is exerted on the passive or noncontractile uterine segment, which lies below the physiological retraction ring and consists of the cervix and lower uterine segment. Thus, the cervix and lower segment are lengthened and thinned (effaced) and finally, dilated. Once begun, dilatation and effacement continue together. The increased hydrostatic pressure developed within the membranes and the downward thrust of the fetus, both the result of the uterine contractions, are additional factors causing dilatation and effacement. When the membranes rupture, the fetal head acts directly as the dilating wedge. The processes begin some weeks before the onset of labor. Preliminary changes in the cervix and lower segment ease the task of dilatation and effacement. These changes soften the passive segment and make it more elastic. They are the result of increased vascularity and edema of this portion of the uterus and are probably also fostered by hormonal changes. The pathogenesis of the prelabor effacement and dilatation differs only quantitatively from that of labor. The longitudinal and circular muscle fibers of the contracting uterine segment contract and retract. Some degree of permanent shortening (brachystasis) results from each contraction and a corresponding amount of permanent progress in effacement and dilatation ensues. When there has been sufficient expansion of the lower uterine segment to accommodate the presenting part, the latter descends in the uterus to fill the newly developed space. As a result the part also descends in reference to the bony pelvis and may engage. This is termed "lightening" and, in normal circumstances, usually occurs 3 weeks or more before true labor.

What are the signs of placental separation?

(1) The presence of strong uterine contractions, (2) a mild gush of blood from the vagina while the uterus is well contracted ("placental sign"), (3) advancement of the cord 7.5 to 10 cm., (4) elevation of the level of the corpus despite a firmly contracted uterus, (5) the presence of a soft, boggy mass below the firm fundus and in the suprapubic area, (6) change in uterine contour from an ovoid to a globular shape.

Give the signs diagnostic of an occiput left anterior position.

Abdominal Signs: Longitudinal lie; firm ridge of the back on the left with anterior shoulder palpable in the left lower quadrant near the midline; palpation of the head (hard, ovoid, ballottable, smooth, movable) over the inlet with the short arm of its fulcrum (the occiput) on the left, superficial, and near the midline, and the long arm (the synciput) deeply placed on the right; palpation of the breech (indistinct, irregular, firm but not hard, not ballottable, not movable separately from the body) in the fundus; audible fetal heart sounds in the left lower quadrant over the anterior shoulder.

Vaginal or Rectal Signs: Identification of the head as the presenting part (hard, smooth, ovoid, presence of sutures and fontanels); saggital suture in the right oblique; posterior or small fontanel anterior and to the left but near the midline.

Describe the mechanism of labor with an occiput anterior position.

As labor progesses and the cervix effaces and dilates, the head descends in the right oblique. As it descends, the long arm of the cephalic lever, the synciput, meets more resistance than the short arm, the occiput, and flexion occurs. As the widest diameter of the head, the suboccipitobregmatic, passes through the pelvic inlet, engagement occurs. As the occiput encounters the curved, sloping inclined plane of the pelvic floor, it is forced anteriorly and to the right, 45 degrees in a counterclockwise direction (internal rotation). With further descent, the occiput passes beneath the pubic arch and delivers. The neck is arrested beneath the symphysis and, acting as a fulcrum, causes the face to sweep across the perineal body and be delivered by extension. The neck, which was twisted as the head underwent internal rotation, now untwists (restitution) and the head rotates 45 degrees clockwise. Meanwhile, the shoulders engage their bisacromial diameter as the head reaches the pelvic floor. Descending in the left oblique, the anterior shoulder is forced further anteriorly as it encounters the pelvic floor. This causes the head to rotate another 45 degrees to the left (external rotation). As descent continues, the anterior shoulder stems under the symphysis. Its delivery is delayed while the posterior shoulder rotates out over the perineum as lateral flexion of the body occurs. The anterior shoulder is then born and is followed rapidly by the rest of the body.

Describe the management of normal second-stage labor.

The second stage of labor begins when the cervix is completely dilated. It may be ushered in by a slight increase in bleeding. Uterine contractions force the presenting part downward. Vaginal distention and pressure on the rectum give the patient a feeling akin to that when a bowel movement is imminent and a reflex develops forcing the patient to bear down. Caudal or saddle-block spinal anesthesia eliminate this sensation and reflex. The patient should be warned of the new sensation that will occur as the second stage approaches so that she will not be surprised by it and, through her surprise, panic. She is urged to rest between contractions and then, as a contraction begins, to take a few deep breaths, hold the last one, and bear down as hard and in as sustained a fashion as possible. Inhalation anesthesia may be given with each contraction to relieve pain and/or promote cooperation and prevent exhaustion. Multipara tend to have a short second stage, hence preparations for delivery are made about the time the second stage begins. Primagravida are usually not prepared until the perineum begins to bulge. Fetal heart sounds are checked almost constantly once the second stage is begun because delivery can usually be carried out promptly with forceps should signs of serious fetal distress develop. Maternal vital signs are also checked at short intervals. The obstetrician and his assistants don caps and masks, scrub, and gown. The patient is usually placed on the delivery table in the dorsolithotomy position, although some obstetricians prefer delivery in bed where the patient can bend her back and bear down more efficiently. The patient is then scrubbed and draped and usually catheterized. If an opiate has been given shortly before delivery, an antagonist may be given. If the patient is dehydrated or there is anything to suggest the development of a maternal complication, a slow intravenous drip of 5 per cent glucose may be started. Blood should always be readily available should it be needed in an emergency. A bassinette is prepared for the newborn.

If any problem is expected with the baby, a pediatrician should be on hand.

Describe the normal physiology of the third stage of labor.

When the fetus is delivered, the uterus rapidly decreases in size. The placenta is inelastic and is partially torn away from its bed, since that area takes part in the general shrinkage. Bleeding develops between the placenta and the uterine wall, and a retroplacental hematoma forms and separates the placenta. The line of cleavage is through the decidua spongiosa. The basalis is left behind to regenerate future endometrium. The membranes remain attached to the placenta and peel from the wall as the placenta drops into the uterine cavity and is delivered. Additional uterine contractions force the placenta out of the cavity, through the cervix, and into the vagina. From these it is delivered by the bearing-down efforts of the patient and/or the gentle downward pressure on the fundus by the physician.

How may abnormality of pelvic configuration affect labor?

While a gross reduction in pelvic size and a severe deformity of the pelvic shape interfere in obvious fashion with the normal mechanism of labor, individual variations in pelvic architecture that are common and that in themselves are unspectacular contribute not infrequently to dystocia. At the pelvic inlet, narrowing of the forepelvis (the prominence of the sacral promontory) prevents efficient utilization of pelvic space and forces the presenting part posteriorly. To compensate for this abnormality, a deep, normally curved posterior pelvis is required to accommodate the posteriorly displaced presenting part. Unfortunately, in a typically android pelvis, a narrowed forepelvis is combined with a shallow, flattened posterior pelvis and, in this circumstance, engagement is accomplished with increased difficulty. In the midpelvis, unusually prominent ischial spines may reduce the transverse pelvic diameter sufficiently to prevent normal passage of the presenting part unless it can be displaced sufficiently anteriorly or posteriorly to offer a smaller diameter of the presenting part to the bispinous diameter. There is usually insufficient anterior space to accommodate this shift, and so an ample or greater than average posterior midpelvic space may be required. The available posterior space depends largely on the width of the sacrosciatic notch and the curvature and posterior angulation of the sacrum. Here again, in the android pelvis particularly, not only are the spines prominent and the bispinous diameter reduced, but the posterior pelvic space is reduced by the presence of a narrow sacrosciatic notch, a straight sacrum, or one in which the normal inner concavity is reduced, and by anterior angulation of the sacrum. At the pelvic outlet, normally available anterior pelvic space is reduced if the subpubic angle is less acute than normal. The narrow pelvic arch, formed by the descending pubic rami, forces the presenting part posteriorly. To compensate in this circumstance, the presenting part must find room in the space between the ischial tuberosities and the sacrum. The amount of space available posteriorly depends on the bi-ischial diameter —a measurement dependent on the subpubic angle and the depth of the pelvis —and the location of the lower sacrum, which will depend on the anteroposterior angulation of the sacrum and the sacral curvature and will be related to the amplitude of the sacrosciatic notch.

What signs or circumstances suggest dystocia due to cephalopelvic disproportion at the pelvic inlet?

Cephalopelvic disproportion is a dynamic problem, at one time developing or potential, at another existent, and finally, in most instances, solved if labor is good.

In early pregnancy, determining that pelvic measurements, both external and more importantly internal, are smaller than average and/or that pelvic shape is abnormal suggests potential cephalopelvic disproportion at term. A history of previous difficult labors and deliveries, of a pelvic accident, or of illness such as rickets or polio that may alter pelvic size and shape also suggests potential trouble.

When the patient is within a few weeks of term or in labor, the failure of the head to engage or descend normally, the existence of an abnormal presentation or attitude, and an estimation that the fetus is unusually large may indicate the presence of disproportion. If the head cannot be engaged or nearly engaged by manual direction and pressure through the abdomen with the thighs flexed (the Müller-Hillis maneuver), or, with the patient in this position, there is more than 1-cm. difference between parallel horizontal planes touching the superior surface of the maternal symphysis and the most prominent spot of the fetal anterior parietal bone, the existence of disproportion is strongly suspected.

When dystocia due to disproportion is anticipated, roentgen pelvimetry should be done within two weeks of the expected labor or during early labor. Direct measurements of the pelvis (and, at times, of the fetal head), study of pelvic shape as shown on the films and a knowledge of the effects of the pelvic shape on the mechanism of labor, clinical and roentgen comparisons of fetal head size and pelvic size, considerations of fetal position and attitude and the malleability of the fetal head, and consideration of the other factors that may be expected to influence labor will aid the experienced obstetrician in deciding whether or not a sufficiently serious degree of cephalopelvic disproportion exists to attempt vaginal delivery.

Because the forces of labor, unpredictable until labor is observed, are an important factor in the solution of borderline problems of disproportion, it frequently happens that no decision can be made before labor demonstrates its ability or inability to overcome the disproportion. Often, the factor of labor can be evaluated in a relatively few hours of observation—a trial of labor. Occasionally, it cannot be solved before the cervix is completed dilated and the effects of second stage labor observed—a test of labor.

Discuss the treatment of cephalopelvic disproportion.

Therapy of cephalopelvic disproportion depends on its diagnosis and an evaluation of its severity. If the degree of its severity is thought to be sufficient to endanger the life or health of the mother or fetus, elective cesarean section is performed at the thirty-eighth week of pregnancy or at the onset of labor. Since this decision is an important one, it should be re-evaluated by a competent obstetric consultant.

When borderline disproportion is present, a test or occasionally a trial of labor is required. Throughout this, the parturient's health must be safeguarded by unusually diligent attention to the signs that indicate her condition and to the general supportive measures designed to guard against infection, fluid and electrolyte imbalance, and general physical and mental deterioration. The safety of the fetus is guarded by watchful attentiveness for signs of fetal distress (e.g., changes in fetal heart rate, the presence or absence of meconium in the vagina if the membranes are ruptured). If signs of distress are evident before vaginal delivery is safe, the labor is interrupted by cesarean section. When and if the progress of a test of labor indicates that safe vaginal delivery cannot be reasonably expected, the labor is interrupted by cesarean section. Again, consultation should be obtained before these decisions are made. If the patient is permitted to reach the second stage of labor, the normal mechanism of labor may result in vaginal delivery. Not infrequently, however, even when safe vaginal delivery can be expected, the parturient requires operative aid, perhaps by rotation of the presenting part or by forceps extraction. The decision for operative intervention, other than that of the simplest type, and the type of procedure require the careful evaluation of a well-trained obstetrician. The method of delivery will depend primarily on the pelvic anatomy, the position and attitude of the fetus, the degree of the disproportion, and the skill and experience of the accoucheur.

What are the values of and the contraindications to the use of oxytocin and ergonovine in obstetrics?

The oxytocic drugs are of important value in obstetrics because of their ability to induce labor, to stimulate hypotonic labor, to aid in the completion of an incomplete or inevitable abortion, to reduce or control obstetric hemorrhage (particularly that due to uterine hypotonia after delivery or associated with or following abortion), and to hasten the involution of the puerperal uterus. In addition, oxytocin has the unique ability to initiate the "let-down reflex" during lactation. The primary dangers of these drugs stem from their ability to stimulate pathologically powerful uterine contractions in the pregnant uterus. These abnormally forceful contractions can rupture the uterus or severely lacerate the lower genital tract as the fetus is propelled forcefully through it. They can also kill a fetus or severely injure it either by affecting the uteroplacental circulation or by the explosive drive with which the contractions force the fetus through the maternal pelvis. Both oxytocics can also cause serious maternal complications in individual cases by their vasopressor effects on the maternal circulation.

Oxytocin has been favored over ergonovine for the induction or stimulation of labor. On the other hand, ergonovine has the advantages of a more prolonged action and of efficacy by mouth.

Contraindications to and safeguards in the use of these drugs in labor are self-apparent. They should never be used unless the obstetrician in charge is present. They should never be used in the presence or suspected presence of a serious degree of fetopelvic disproportion. Abnormal fetal presentations or attitudes suggest the unrecognized presence of disproportion. In the presence of mild borderline disproportion, they should be used, if at all, with the utmost care. In this situation, as when they are employed to treat hypotonic uterine inertia, the contractions that result from the stimulation should not be more forceful than normal contractions. Furthermore, these drugs should never be used to stimulate an exhausted uterus before it is rested. They should not be employed or must be used with unusual care in instances in which the integrity of the uterine wall is uncertain, for example, in women who have borne a number of children, in patients who have had a previous cesarean section or myomectomy, and possibly in the presence of placenta praevia or abruptio placentae. It has been suggested that their use be avoided in the type of case in which the incidence of thromboplastic or amniotic emboli is unusually frequent, e.g., in the presence of a dead fetus or placental abruption. They are usually contraindicated in the presence of signs of fetal distress or when the fetus is suspected of being unusually fragile. The oxytocic drugs aggravate hypertonic uterine inertia and should be avoided, therefore, in this type of case. Whether or not they should be used in the third stage of labor is a debated question. Those who say they should not fear that the resultant forceful contractions may entrap the placenta in utero.

The cardiovascular complications that may occur after the use of oxytocin and ergonovine stem from a contaminant in the former and an inherent quality in the latter. The danger of coronary-artery spasm from impure oxytocin may contraindicate its use in patients under general anesthesia. Both drugs may produce hypertension, occasionally of a serious degree. This untoward reaction is prone to occur most frequently in patients who have latent or established hypertension. It is well, therefore, to avoid them in this particular group of patients, especially during the immediate postpartum period.

The inauguration of a method by which oxytocin is given intravenously in very dilute solution has added to the safety with which this drug can be given by making it possible to inject and use a very small amount of the drug at a given moment of time and by furnishing a method by which continuing dosage is easily controlled.

What are the potential problems of prolonged pregnancy?

About 10 per cent of pregnancies continue past the forty-second week and 5 per cent, past the forty-third. Most of these prolonged gestations present no special problem. In certain instances, however, both fetal and maternal morbidity and fetal mortality rates rise because of circumstances associated with or due to the prolongation. When these special problems occur, they are rarely important until after the forty-second week. The first problem to be solved when the patient passes her expected date of confinement is whether or not a miscalculation is involved. A number of women do not keep accurate records of menstrual dates and others may forget and then guess at dates of specific developments that are observable in pregnancy and helpful in orienting maturity. Menstrual irregularities offer another opportunity for error in calculations of term. One must use every conceivable method and then correlate the results carefully before passing judgment on prolonged pregnancy, particularly if the judgment suggests a need for interference.

Once the diagnosis of prolonged pregnancy is made, the obstetrician should be aware of two potential and important complications. The first comprises a group of problems that may be expected when one encounters an unusually large fetus with increased calcification of the skull bones. These are the complications associated with cephalopelvic disproportion. Decisions and therapy follow the precepts determining the care of patients with disproportion.

The second problem is that of placental insufficiency, which in these cases is the result of placental senescence. The insufficient placenta may be encountered in pregnancies and labors even before term, so this problem is not a unique one in prolonged pregnancies. It is more common, however, in pregnancies that go beyond the forty-second week. The problem stems from the inadequate transfer of essential materials from the mother to the fetus through the placenta. Oxygen is the most important of these "essential elements" to the fetus in a prolonged pregnancy. Fetuses comprising this group are normal in size or, often, less than normal size. There is little or no trouble, therefore, in distinguishing potential candidates for this group and those comprising the first. Usually, although not always, oxygen transfer is sufficient to maintain life until labor begins. Then, pressure changes in the uterine wall produce circulatory changes in the maternal placental circulation that interfere with oxygen transfer to the fetus. A slight decrease in oxygen may result in a degree of hypoxia fatal to the fetus. A constant and careful alert for signs suggesting fetal distress must be kept throughout the labors of all cases that may be in this group; should signs of fetal hypoxia appear, immediate delivery is mandatory. This may require cesarean section.

There is a special, rare subgroup of cases of placental insufficiency that require particular care. These cases are diagnosed by past history and by exclusion. When a patient has lost two or more fetuses either during or shortly before labor and no cause for these deaths was apparent, the presumptive cause of death is placental insufficiency. These cases should be sectioned electively before the critical time of loss as indicated by the patient's history.

If one is sure of the expected date of confinement, it is probably sound obstetrics to induce labor in pregnancies continuing beyond the forty-second week, if all the criteria for safe elective induction are fulfilled. Unfortunately, even this precaution will do little to solve the two serious problems of prolonged pregnancy. Usually the criteria for safe induction are not fulfilled in these very cases that would benefit by it. Attempts are being made to determine, scientifically, placental, and thus fetal, size, weight, age, and health by laboratory methods. These may furnish real and important help but insufficient experience prevents the accuracy of their prognostic values. These methods include studies of vaginal-smear cytology and hormonal titrations. It is true that postmature placentas have very high progesterone and low estrogen contents. These changes are reflected in the peripheral blood and urine. Current study centers around the correlation of serial urinary estrol and/or pregnandiol values with fetal prognosis. There is no doubt that these tests can give us information about placental function and physiology. At least in some cases, fetal danger from placental inadequacy can be predicted and help furnished in determining the time of critical reduction in placental transfer. These research studies give promise of furnishing us with important information on which to base rational therapy for these cases.

List the indications for cesarean section.

Contracted pelvis with fetopelvic disproportion; abnormalities of uterine contractility and conduction that obtain inadequate or incomplete cervical dilatation (uterine inertia); hemorrhage endangering the mother and/or the fetus at a time when vaginal delivery is too distant to await with safety (placenta praevia or placental abruption); toxemia that cannot be controlled by medical therapy and exists in a patient unprepared for a trial of labor; a rapidly decreasing number of conditions appertaining to coincidental medical disease, e.g., in the presence of certain complications incident to diabetes in which premature delivery is indicated when the patient is not ready for safe induction of labor; certain abnormalities of presentation, particularly transverse lie; fetal distress, including certain cases of prolapse of the umbilical cord, in which there is a significant danger to fetal life at a time when delivery is not imminent; infrequently in special instances of Rh negative sensitization; previous cesarean section done for an indication no longer existent and in which the integrity of the uterine scar is the subject of reasonable doubt; in some clinics, previous cesarean section done for any reason and under any and all circumstances; the coincidental presence of a successfully repaired vesicovaginal fistula or successful sling operation for urinary incontinence; the proved existence of invasive cervical cancer; the presence of a pelvic tumor blocking the pelvic passages traversed by the fetus.

As surgical operations have become safer and safer, the indications for cesarean deliveries have been expanded. This liberalization has included particularly indications or circumstances that, while safe for the mother, would in the past have exposed the fetus to serious danger if vaginal delivery had been accomplished. Thus such combinations of circumstances as toxemia, abnormal presentations, or incoordinate uterine activity existent in patients who have had sterility problems or who are elderly primigravidas; diabetes in a gravida with a poor obstetric history; questionable disproportion; a poor labor; and borderline cases of obstetrical hemorrhage or postmaturity in which signs of fetal distress suggest moderately, but without certainty, danger to fetal life have swelled the list of indications favoring cesarean sections over vaginal deliveries. Broadening of the indications for cesarean section has not significantly increased maternal mortality and morbidity rates and has resulted in a very real improvement in fetal salvage rates.

Discuss the obstetric care of a patient who has had a previous cesarean section.

During the antepartum period, data are assembled about the previous cesarean operation—the circumstances leading up to it, the indication for it, the type of operation done, the condition of the uterus and patient at the time of operation, and details about the postoperative convalescence. At the same time, the current pregnancy is carefully evaluated. As term approaches and when a trial of labor is contemplated, the adequacy of the pelvis is proved by roentgenographic pelvimetry, the location of the placenta is determined by appropriate x-rays, and the probable character of the anticipated labor is predicted by such developments as the antepartal preparation of the lower uterine segment and cervix and the descent of the head. Signs and symptoms of impending rupture of the uterine scar—an uncommon occurrence more frequent in corporeal than low segment operations—are watched for alertly.

In many clinics, the dictum "once a cesarean, always a cesarean" is followed in unwavering fashion. On an increasing number of obstetric services, the decision whether to attempt vaginal delivery or again resort to cesarean section after a previous cesarean section is individualized. All obstetricians agree that, if the indication for the first operation is still existent (e.g., contracted pelvis with fetopelvic disproportion), a repeat cesarean is essential. If, however, the indication for the first cesarean section was limited to the pregnancy that it was used to terminate (e.g., fetal distress caused by a prolapsed cord), many obstetricians prefer to give the patient a carefully supervised trial of labor in her following pregnancies. This is particularly true if the patient is parous. These obstetricians who individualize their cases permit labor and expect vaginal delivery if the circumstances surrounding the operative delivery—that is, the condition of the patient and her uterus, the care with which closure of the uterine wound was accomplished, and the patient's course following the operation (presence or absence of unexplained fever or pelvic complications)—predicate the presence of a strong and healthy uterine scar, if there are no signs or symptoms of impending uterine rupture, if signs near term prognosticate that the anticipated labor will be normal, if the placenta does not overlie the uterine wound, and if the patient is willing to attempt labor.

What are the signs and symptoms that suggest rupture or threatening rupture of a uterine scar? What are the dangers of such a rupture?

The signs and symptoms of threatening or partial rupture of a uterine scar are not clear-cut and, in the early phases, are difficult to interpret as diagnostic sign posts. They include disproportionate visceral pain and tenderness in the area of the uterine scar, hematuria and/or bladder tenesmus, unexplained failure or interruption of descent of the presenting part, unexplained vaginal bleeding, unexplained signs of fetal distress or even fetal death, and a palpatory defect in the uterine wound. This last sign is possibly the least satisfactory of all, since definite defects are easily missed and what is thought to be a defect may prove to be an artifact. The patient's intuition has been listed as an additional sign. If complete rupture of the scar occurs, the same symptoms are present in more dramatic fashion; in addition, a gaping hole in the uterine wall may be easily palpated; the presenting part may appear superficially beneath the abdominal wall; labor may stop; there may be signs and symptoms of internal or occult bleeding.

The greatest dangers from uterine rupture are fetal death and the possible need for hysterectomy because the uterine tear does not lend itself to repair. Maternal blood loss is usually not so acute as to endanger the mother's life before it can be corrected by transfusions. The complications are potentially serious, but are fortunately uncommon. In deciding for or against repeat cesarean section, the dangers from the complications incident to wound rupture must be balanced against the very real increase in maternal morbidity and mortality rates—however, also gratifyingly low—incident to repeat cesarean section.

Outline the diagnosis of breech presentation.

Abdominal Examination: The lower pole of the fetus is soft, irregular, and easily displaceable above the pelvic inlet. The upper pole is hard, smooth, spheroid, and ballotable. The latter moves independently of the trunk. The anterior shoulder is palpated below it. Fetal heart sounds are heard above the umbilicus.

Rectal and Vaginal Examinations: The presenting part is frequently high and the pelvis empty. It is not the hard, globular head with its usual distinguishing features but rather a soft, irregular mass in which the anus, genitalia, sacrum, and tuberosities are identified. The lower extremity may be palpable.

Name three methods of managing the aftercoming head in breech delivery.

Mauriceau-Smellie-Veit Method: The trunk of the baby is placed astride the left arm of the operator and the middle finger of the left hand is placed in the fetal mouth, while the adjacent fingers grasp the shoulders. The middle finger of the right hand presses upon the occiput while the other fingers grasp the shoulders dorsally. As flexion is maintained the head is drawn down along the pelvic axis until the occiput stems beneath the symphysis. The trunk of the infant is then lifted upward and the head is born as the chin, mouth, etc., sweep over the perineum.

Wigand Method: The use of the left arm is the same as that described above, but the right hand aids in the delivery by suprapubic pressure.

Piper Aftercoming Head Forceps: After one or both of the above methods have been unsuccessfully attempted once, forceps should be promptly applied. The head must be engaged when this is done. The trunk and extremities of the infant are held up out of the way by an assistant. The blades are inserted along the lateral pelvic walls. Traction is downward and outward until the occiput passes beneath the symphysis and then the handles are brought upward in an arc to accomplish the birth of the head as in the manual maneuvers.

What are the causes of face presentation?

Face presentation is usually a secondary development from a vertex presentation. It is caused by any pathology which prevents or interferes with flexion of the head. Neck tumors (thyroid), coils of cord around the neck, or abnormal elongation of the posterior portion of the head (dolichocephaly) are fetal causes. Contributing maternal factors are usually due to a faulty uterine axis (pendulous abdomen with anterior or lateral corporeal displacement).

What is uterine inversion? Name the causes and outline the therapy.

Uterine inversion is a condition in which the uterus is turned inside out, either partially or completely. It may occur spontaneously or be due to traction on the umbilical cord or injudicious attempts at placental expulsion. Severe shock and hemorrhages usually occur.

The *diagnosis* is made by vaginal examination.

Management consists in treatment of the postpartum hemorrhage and shock and the manual replacement of the fundus by a hand in the vagina. Deep anesthesia and adrenalin aid in the manual replacement. If the uterus cannot be replaced by this method, one of two surgical approaches may be employed after the shock and hemorrhage have been controlled. The abdomen may be opened and the fundus replaced by traction on clamps attached to it. Vaginally, the cervix and lower corpus can be incised anteriorly, the uterus replaced, and the incision sutured (*Spinelli operation*).

What are the dangers of traction on the umbilical cord?

Rupture of the cord; premature partial separation of the placenta; inversion of the uterus.

What is postpartum hemorrhage? Name the types and causes. Outline the therapy.

The term "postpartum hemorrhage" as commonly employed means excessive bleeding after the delivery of the baby. In a purist sense it refers only to such loss after the completion of the third stage. It may be immediate (within the first 24 hours postpartum) or delayed. The latter is a separate problem and is not discussed here. The former is of two main types: that from the placental site (atonic hemorrhage) and that from lacerations of the birth canal. The atonic type is most frequently caused by faulty management of the third stage (i.e., roughness, too early attempts at placental expression, traction on the cord). It may also be due to uterine inertia, deep anesthesia, retained placenta or placental fragments, placenta praevia or placental abruption, fibroids, too rapid delivery, or to unknown factors. If bleeding occurs when the uterus is well contracted it is probably from a laceration. The best therapy is prophylaxis: attention to the patient's general health not only in labor but during the antepartum period; correct management of delivery and the third stage of labor; avoidance of trauma to the mother on the delivery table. When hemorrhage occurs, therapy is designed to stop the bleeding, combat shock, and replace blood loss. In atonic hemorrhage, bleeding can usually be controlled by lifting the uterus out of the pelvis into the abdomen and gently massaging the fundus (see management of third stage). If the placenta has been delivered, an oxytocic will probably help the uterus to contract firmly. If the hemorrhage persists and the placenta or one of its fragments is still within the uterus, the placental tissue should be manually removed. If the bleeding cannot be controlled, the uterus and vagina should be packed (uterine tamponade). Finally, if these measures fail, hysterectomy is necessary. Bleeding from lacerations is best treated by their repair. If this is not feasible, temporary hemostasis may be obtained by packing. Meanwhile, in all types of bleeding shock must be combated. This is best accomplished by whole blood transfusions. After the bleeding is controlled, the patient must be carefully watched for at least several hours to ensure against a repetition of hemorrhage.

Discuss the cause and prevention of puerperal sepsis.

The disease depends upon the presence of virulent or potentially virulent bacteria in the genital tract. These may enter the parturient canal from: (1) a distant focus of infection in the patient; (2) contamination from outside sources prior to or during labor, e.g., douches, unsterile or multiple vaginal or rectal examinations, respiratory-tract infections of attendants; (3) soiling during labor, e.g., improperly sterilized instruments and linens, faulty aseptic technique of the obstetrician, operative manipulation; (4) poor postpartum technique. Even though offending bacteria are present, their growth and spread will be inhibited by the general and local resistance to infection of the patient. The protection furnished by these natural barriers is not only altered by the patient's general health but is weakened by such factors as long labor, premature rupture of membranes, invasion of the genital tract, and particularly by traumatic obstetric interference.

Prevention of sepsis becomes evident from a study of its causes. It consists of many factors, among which are good antepartum care, the employment of aseptic technique, careful evaluation of each patient in order to prevent the need for traumatic delivery, avoidance of unnecessary invasion from the genital tract, and prevention of needless patient contact with known or potential sources of infection. The chemotherapeutic and antibiotic agents, particularly penicillin, given prophylactically at the time of unavoidable complications, such as premature rupture of the membranes and long, inert labors, have materially aided in reducing puerperal morbidity.

List the indications for the interruption of pregnancy.

Many indications have been given for the interruption of pregnancy. None is absolute and the factors in a particular case are decisive of the need for and merits of interruption. Particularly in the group of diseases accidental to pregnancy and in the toxemias, the trend is toward prophylaxis and/or careful medical control during the antepartum period rather than toward interruption. Among the classic indications for abortion or premature induction of labor are the following:

(1) *Causes peculiar to pregnancy:* toxemia (early and late), hemorrhage (placenta praevia, abruptio placentae), habitual fetal death, polyhydramnion, hydatid mole, erythroblastosis fetalis.

(2) *Causes accidental to, but aggravated by, pregnancy:* cardiovascular and renal diseases, pulmonary tuberculosis, diabetes, certain blood and nervous and mental diseases.

(3) *Cephalopelvic disproportion,* especially that due to postmaturity.

How should a patient who is pregnant and is found to have cervical carcinoma be treated?

Intraepithelial carcinoma is treated differently from invasive cervical cancer. Once its presence is suspected from a cytological smear or punch biopsy, the diagnosis must be confirmed by a cold knife biopsy-excision of the cervical portio (see question in gynecological section, p. 492). If no invasive cancer is found, it is recommended that the pregnancy be left undisturbed and the patient followed during the antepartum period with smears and, when the need is suggested by positive smears, additional biopsies. At term, unnecessary cervical trauma should be prevented by delivery by cesarean section. After delivery, the patient must be followed with periodic cytological smears and/or cervical biopsies. An added precaution, even if smears remain negative, is to rehospitalize the patient at the end of the puerperium for another cold knife excision of the cervical portio and curettage of the endocervix for diagnostic purposes. Subsequent treatment depends on the results of follow-up studies and one's philosophy about the disease. The histological diagnosis of intraepithelial cancer is difficult and it depends on the services of an expert pathologist. A picture simulating intraepithelial cervical cancer is frequently encountered during pregnancy and is difficult for any but the expert to differentiate.

The treatment of cervical cancer is far from standardized. Some experts will no doubt disagree with the regimen just outlined for intraepithelial cancer and that which will be suggested for the treatment of invasive cancer. One realizes that time, new developments, experience, and changes in one's personal philosophy may make some other form of treatment more acceptable in some clinics and under certain circumstances. The methods suggested in this answer include one acceptable method but not necessarily *the* method for the treatment of this situation.

The treatment of invasive cervical cancer associated with pregnancy must begin with the diagnosis of the cancer. All suspicious cervices must be biopsied (this can be done safely and without disturbing the cervix) and, when possible, investigated by cytological smears. Whenever bleeding occurs in pregnancy, the cervix should be visualized and palpated without undue delay. Once the diagnosis is established, treatment depends on the duration of the pregnancy, the clinical extent of the disease, and the method of treatment of cervical cancer preferred by the therapist in charge. Several generalizations can be made. The pregnancy should be terminated, unless unusually early, by the abdominal route—either by hysterotomy or cesarean section—so as to avoid unnecessary cervical trauma. Unless moral or religious scruples interfere, a previable pregnancy and probably one of less than 28 weeks should be terminated promptly and appropriate definitive therapy, either with radiation or radical surgery or both, should be carried out as soon as possible. If the time of pregnancy is approaching when the delivery of a healthy baby can be expected without undue delay—some limit this delay to as short a period of time as one month—it seems justifiable in the interests of the baby and without unduly jeopardizing the chances of maternal cure to await the appropriate time, deliver the baby by cesarean section, and follow delivery immediately or as soon as possible with the definitive therapy of choice.

Give the techniques for therapeutic abortion.

Pregnancies of 12 weeks or less are usually terminated by D. and E. The cervix is dilated and the ovum removed piecemeal with an ovum forceps. Thereafter, the uterine cavity may be lightly curetted. Also, it may be packed, either to control bleeding or ensure emptying on removal of the packing in 12 or 24 hours. The chief dangers of D. and E. are hemorrhage and instrumental perforation of the uterus. Abdominal hysterotomy, or, in special instances, hysterectomy is usually used for therapeutic abortion after the twelfth week. These operations can be done vaginally. Some obstetricians terminate pregnancies between the eighth and sixteenth weeks by a combined method. The cervix is packed, oxytocin is given intravenously, membranes are ruptured, and finally the procedure is carried out as in D. and E., after the uterus has partially emptied itself. Abroad, abortions of pregnancies of more than 10 weeks are often performed by injecting a solution of cremor saponis into the uterus. This technique has not found acceptance in this country.

List the indications for obstetrical forceps.

To aid the expulsive power of the uterus (uterine inertia, mild cephalopelvic disproportion); to rotate or flex the head (malpresentations or positions); to aid in the rapid termination of labor in the presence of maternal or fetal crises (cardiac decompensation, prolapsed cord); to shorten labor electively and thereby prevent fetal injury, maternal pain, and maternal exhaustion, particularly in the presence of systemic maternal disease; to control delivery and thereby lessen maternal and fetal trauma.

What are the rules to be observed for the proper use of forceps?

The presenting part must be the head and there must be an indication for the use of forceps. The cervix must be completely dilated and effaced. The head must be engaged and the presentation and position known with certainty. No cephalopelvic disproportion, or at most no more than a minor degree of it, must exist. The membranes must be ruptured and the bladder empty. The principles of aseptic technique must be carefully followed and, except in exceptional circumstances, the patient must be anesthetized. Forceps are contraindicated if these criteria are not fulfilled. They should not be used to attempt an impossible delivery, such as occurs with a mentum posterior position.

What is a version? Name the types.

Version is the manipulation by which the fetus in utero is turned and the presenting part thus changed. When the version changes the fetus to a cephalic presentation it is called “cephalic”; when to a breech, “podalic.” Version is further described as external, internal, or combined, depending upon the approach employed.

List some of the indications for placing the fingers or hand in the uterine cavity. What precautions must be taken?

To extract a retained placenta; control profuse, postpartum hemorrhage; aid in diagnosis of position or presentation; determine the presence of a suspected uterine tear; correct malpresentations or positions; perform breech decomposition or version; search for and remove placental fragments; replace a prolapsed, pulsating cord; detect the presence of a lateral placenta praevia; strip the membranes in induction of labor.

The procedure must be done with strict aseptic technique. Anesthesia is frequently required. Penicillin may be used prophylactically if the associated factors indicate the danger of subsequent infection.

Discuss syphilis in pregnancy.

Syphilis is a dangerous complication of pregnancy, even though it is a less acute illness in women than men and is further attenuated by pregnancy. If the infection is acute and untreated in early pregnancy, the fetus is usually overwhelmed by spirochetes in the second trimester, dies, and is aborted. Without therapy, the same course of events occurs in subsequent pregnancies but the abortions become later and later, and often, finally, a live baby but one involved with congenital syphilis is obtained. Infection occurring late in pregnancy may not cross the placental barrier and the fetus may be spared. Adequate therapy is 6,000,000 U. of aqueous penicillin G given in divided doses over a period of 10 consecutive days. The penicillin crosses the placental barrier and cures the fetus, too, if it is involved. If the patient has been adequately treated with normal response, retreatment in pregnancy is not necessary unless there is evidence of clinical or serological relapse. The diagnosis of syphilis in the mother is made as in the nonpregnant. Usually it is done by serological test, a test that should be done routinely in early pregnancy. Some repeat the test routinely in the second half of pregnancy, particularly among groups of patients who have a higher than average incidence of the disease.

Discuss the diagnosis of placenta praevia.

Symptoms: Painless, causeless vaginal bleeding, occurring characteristically in the last trimester of pregnancy. Recurrent bleeding, usually in progressively larger amounts. Bloody, serous discharge between episodes of bleeding. Labor may begin with subsequent hemorrhage. Symptoms of blood loss.

Signs: (1) *Vaginal:* intrauterine bleeding; palpable placenta. (2) *Abdominal:* normal, possibly irritable uterus; floating presenting part; possible malpresentation; low-lying placental souffle. (3) *General:* signs of blood loss compatible with visible bleeding. (4) *Laboratory:* x-ray visualization of low-lying placenta or absence of placental shadow in visible mid- or upper uterus.

What is abruptio placentae and what are its causes?

Abruptio placentae is the premature separation of a normally implanted placenta. It is due to: (1) toxemia of pregnancy; (2) trauma (including forceful extra- or intrauterine manipulations); (3) miscellaneous causes (sudden reduction in uterine size after rupture of membranes or delivery of the first of twins; traction on a short umbilical cord).

Classify the toxemias of pregnancy.

The following classification was suggested in 1952 by the Committee on Maternal Welfare: (1) Acute toxemia of pregnancy, (a) pre-eclampsia, (*1*) mild, (*2*) severe; (b) eclampsia. (2) Chronic hypertensive (vascular) disease in pregnancy, (a) chronic hypertensive vascular disease without superimposed acute toxemia, (*1*) the cases in which hypertension was known to exist before the onset of pregnancy, (2) cases of hypertension before the twenty-fourth week; (b) chronic hypertensive vascular disease with superimposed acute toxemia. (3) Unclassified toxemias.

Define the criteria for diagnosing the toxemias of pregnancy.

Pre-eclampsia: Systolic blood pressure of 140 mm. Hg or more, or diastolic pressures of 90 or above, that develop after the twenty-fourth week of pregnancy and are evident on two or more occasions, 6 or more hours apart, characterize the blood-pressure change of this complication. "Significant" proteinuria is the second sign. "Significant" usually means more than 1 gm. of protein per 24 hours. Water retention completes the diagnostic triad. No rule exists for definite criteria to separate mild from severe pre-eclampsia. Severe pre-eclampsia might be defined as present when the patient requires hospitalization and more therapy than rest, sedation, and dehydration. One might add that the blood pressure in a severe case is higher than in a mild case and averages in the range of 160 to 180/110 to 120 mm. Hg. Proteinuria in the range of 4 or 5 gm. per 24 hours is usually indicative of severe pre-eclampsia. Symptoms from the pre-eclampsia also tend to put it in the "severe" group.

Eclampsia: This disease is characterized by convulsions or coma in a pregnant or puerperal patient who exhibits hypertension, albuminuria, and edema.

Chronic Hypertensive Vascular Disease with or without Pre-eclampsia: A patient with uncomplicated chronic hypertensive vascular disease has a blood pressure of 140/90 mm. Hg or more prior to the twenty-fourth week of pregnancy and after pregnancy has terminated. Renal function is normal. No water retention is superimposed upon the chronic vascular disease. The systolic pressure rises 30 or more mm. Hg after the twenty-fourth week, and/or the diastolic, 15 mm. Hg or more, and/or "significant" albuminuria develops.

What is the cause of pre-eclampsia and eclampsia?

No one knows the etiology of these diseases. They are unique to pregnancy, requiring trophoblastic tissue for their development—a fetus is not essential. Climate and nutrition influence their incidence. Primigravidity, multiple pregnancy, hydatidiform mole, and chronic vascular hypertension predispose to their development. An interesting theory to explain eclamptogenic toxemia suggests that degeneration or dysfunction of trophoblastic tissue releases or produces a toxic, pressor substance that is discharged into the maternal blood stream. This substance in turn causes vasospasm, hypertension, tissue hypoxia, tissue damage, etc.—the developments of eclamptogenic toxemia. The trophoblastic injury is blamed on reduction in blood flow in the placental bed. In turn, the reduction in blood flow is accredited to mechanical or functional (autonomic imbalance) causes. Other theories emphasize the possible roles of altered steroid metabolism, autolysis of infarcts, dietary deficiencies, thyroid and pituitary disorders, and a variety of other theoretical dysfunctions.

Summarize the treatment of the eclamptic patient.

Every effort should be made to prevent a patient with pre-eclampsia from becoming eclamptic. If the latter is imminent, medical therapy having failed (see earlier question), the pregnancy should be terminated promptly and certainly. This may require cesarean section. Increasing or persisting hypertension of 170 mm. Hg or more, proteinuria of 3 gm. or more per day, and progressive water logging despite active therapy give warning that eclampsia may develop at any time. Signs and/or symptoms of decreasing urinary output, progressive nitrogen retention, blood concentration, progressing abnormality in other blood electrolytes, evidence of developing hepatic or cardiac failure, progressive stupor, severe headaches, and the onset of gastrointestinal and ocular symptoms are equally ominous. If important conservative therapy cannot be added to turn the tide when these developments are at hand and fail to regress in a reasonably short period of therapy, termination is probably the better part of valor. Once eclampsia has developed, the patient needs constant nursing surveillance, a continuing record of clinical signs and laboratory data, and frequent evaluations by the physician. Intake and output records are facilitated by an indwelling catheter. Protection must be afforded during convulsions. A quiet environment is essential to reduce external stimuli. The air passages must be kept clear, frequently by aspiration. Oxygen therapy is given constantly, or at least if there is any cyanosis. Signs of cardiac failure are treated appropriately. In the presence of convulsions, hypertonic (50 per cent) magnesium sulfate is usually given intramuscularly for its sedative-anticonvulsant action. Morphine is used to control painful stimuli if the patient is in labor. The barbiturates, chloral hydrate, and paraldehyde are also among the sedative-anticonvulsants that have proved useful. Hypertonic glucose, usually in 20 per cent solution, is used to promote diuresis. Fifty per cent glucose is substituted if strict curtailment of fluid is indicated. Caudal or spinal analgesia is used not only to reduce blood pressure but to encourage diuresis. It has the added value of being able to eliminate the pain of labor. The antihypertensive drugs are usually used in combinations. Reserpine, hydralazine (Apresoline), and cryptenamine acetate (Unitensin) and the other veratrum derivatives are among the most commonly used of these drugs. New ones are being introduced and evaluated constantly. The aim of this fraction of the regimen is to reduce vascular spasm and thus to reduce the blood pressure to low hypertensive levels and improve tissue oxygenation. Elective termination of a pregnancy during the convulsive phase is usually frowned upon. Nonetheless, it may be life-saving in selected cases. There is agreement about terminating a pregnancy after the convulsive stage is controlled. Evacuation of the uterus is the only cure for eclampsia.

Present the problems incident to the diagnosis and treatment of an ovarian neoplasm associated with pregnancy.

In early pregnancy, an enlarged, tender, cystic ovarian mass is expected. This is the corpus luteum of pregnancy. For this reason, ovarian cysts of reasonable size are not operated upon, save in emergencies, in the first trimester of pregnancy, since one might be operating on the physiological cyst that is essential to the maintenance of the pregnancy. Even neoplastic cysts, diagnosed with certainty, are usually left alone in early pregnancy, unless acute problems occur, because removal of the cyst might inadvertently remove the corpus luteum of pregnancy, which could be present in the same ovary as the neoplasm and might be hidden by the tumor. One must remember that any tender, cystic adnexal enlargement of no more than moderate size may be an ectopic pregnancy when associated with suggestive signs and symptoms of pregnancy. The differential diagnosis between a corpus luteum and an ectopic may be difficult in early pregnancy because the pregnant corpus luteum may be fairly large, spontaneously painful, and quite tender, and the uterus may show the mild suggestive signs of pregnancy. Careful history, observation, and repeated examinations will help clarify the correct diagnosis. Culdoscopy may be helpful in making the correct diagnosis. As a rule, the diagnosis of a significant, neoplastic ovarian cyst accompanying early pregnancy is not difficult. The diagnostic features parallel those by which the diagnosis would be made in the absence of pregnancy. In the younger age group, the most common neoplastic cyst one might encounter is the dermoid. The free mobility offered by its long pedicle and the tendency of dermoids to float anteriorly are helpful diagnostic aids. Just as in the nonpregnant state, ovarian neoplasms may be missed and attention may be centered on them only by intercurrent complications. The long pedicle of the dermoid makes this cyst particularly prone to the complication of torsion. This may cause intermittent pain from ischemia. A severe torsion may produce progressive signs of a surgical abdomen because of the serious strangulation of the blood supply that may occur and the inevitable developments that would follow this complication. Rupture of neoplastic cysts may or may not cause symptoms sufficiently severe to call attention to the presence of the neoplasm.

As pregnancy progresses, the physical diagnosis of a neoplastic cyst may become increasingly difficult, and, for a time, impossible. This is because the tumor is drawn up out of the pelvis beyond the reach of the examining, vaginal hand. At the same time, the cyst may be hidden behind the growing uterus. On the other hand, it may become readily evident for the first time as it is displaced out of the pelvis into the free peritoneal cavity. Although, as a rule, the growth of ovarian cysts is not hastened by pregnancy, it seems to be occasionally. Furthermore, the congestion of pregnancy and the interference with blood supply that may be incident to a gestation may increase the diameter of the cyst. Both situations tend to make the diagnosis easier. Generally the cyst is palpable above and lateral to the pregnant uterus. Its shape and consistency suggest the correct diagnosis even when the cyst is immobilized against the expanding uterine wall. It must be remembered that an ovarian cyst may hide a pregnancy as well as mimic one by its centrally placed, anterior, cystic enlargement. Serial examinations will clarify the diagnosis if original doubt is present. Solid ovarian tumors are infrequent, at least in the younger age group of gravida. Unless the tumor is sizable, its diagnosis is probable only in early pregnancy when it is in the pelvis and in the characteristic adnexal position, apart from the uterus. Differentiation from a subserous pedunculated myoma presents the greatest difficulty. In early pregnancy differentiation is aided by the changing relationship of the tumor to the uterus. Later, such a change is not so overt and, if in a palpable position, the solid ovarian tumor may go unidentified and be considered as a myoma. Although complications of some ovarian cysts—torsion and rupture—are more common in pregnancy than in nonpregnancy, the same background logic and criteria that influence both the diagnosis and therapy of ovarian neoplasms in the nongravid remain unchanged in pregnancy, save for minor exceptions. The first exception, concerning first-trimester operations, has been mentioned. The second is that neoplastic cysts diagnosed near term may await postpartum removal. The short time interval of waiting cannot prove costly. If delivery is awaited, the neoplastic cyst should be removed immediately after delivery. Spatial changes incident to delivery might trigger complications. Incidentally, ovarian neoplasms may be discovered first after delivery because of the ease of palpation of abdominal masses through the relaxed abdominal wall. The rule guiding the therapy of an ovarian neoplasm dictates removal or exploration of the tumor as soon as is practical after diagnosis. This is influenced more by the potentiality of any ovarian neoplasm to become or to be malignant than to any other complications that may involve the cyst. Ovarian cancer is not a rarity among women of childbearing age. The above, cardinal rule, therefore, should not be broken.

List the dangers of toxemia of late pregnancy.

Maternal: Abruptio placentae; vascular accidents (intracranial); aggravated renal disease (at least in some types); sepsis; eclampsia (tongue injuries, pulmonary edema, aspiration pneumonia, death).

Fetal: Prematurity; immaturity; asphyxia; narcosis (from drugs); injuries due to traumatic delivery.

What is false labor and how can it be distinguished from true labor?

False labor is a transient episode of painful uterine contractions, usually occurring near term and having the following characteristics: The pains stop before there is any significant change in the status of the cervix. The progression of frequency, duration, and intensity of the contractions, which is typical of true labor, is lacking. Usually the pains are milder and more irregular. A bloody show or rupture of the membranes rarely occurs. The diagnosis is made by observing the patient over a period of time and noting the above distinguishing features. It is confirmed by cessation of the pains.

Name some of the causes of vaginal bleeding during pregnancy, labor and the puerperium.

Incidental maternal disease, such as aplastic anemia, or cervical disease such as a polyp, erosion, or carcinoma, may cause bleeding at any time during pregnancy or thereafter. Abnormalities of pregnancy that may cause bleeding are:

Antepartum: Abortion, placenta praevia, abruptio placentae, or partial placental separation, ectopic pregnancy, "bloody show," hydatid mole, chorioepithelioma.

Intrapartum: Cervical dilatation, placenta praevia, abruptio placentae or partial placental separation, lacerations of the birth canal.

Postpartum: (1) IMMEDIATE: uterine atony, episiotomy, laceration of the birth canal, inversion of the uterus. (2) DELAYED: subinvolution, retained placental remnants, chorioepithelioma.

Give the criteria by which maturity of pregnancies are determined and by which legal and scientific reports are prepared.

The reporting of births is governed by the laws of the individual states, and these laws vary from state to state. The reporting of obstetrical data by individual hospital services suffers from the same variability of regulations. In general, the data in the table below give average figures in common use. The final decision of estimated age is based on agreement of two of the three criteria, estimated age, fetal weight, and fetal length.

TYPE OF DELIVERY	ESTIMATED DURATION OF PREGNANCY, WEEKS	FETAL WEIGHT, GM.	FETAL LENGTH, CM.
Abortion	<22	<500	<28
Immature	22–27	500–999	28–35
Premature	28–36	1000–2499	36–47
Mature	37–43	2500–4499	48–54
Postmature	>44	>4500	>55

The commonest variables among the criteria listed above involve the upper limit of abortion and the lower limit of prematurity. Four hundred grams and even 250 gm. (16 weeks) are used in some systems as the dividing line for reporting abortions in contrast to immature births. Twenty-six weeks instead of 28 weeks may be used as the time separating premature and immature deliveries.

Why is "bacteremic shock" a serious complication primarily of mid-trimester abortion? How is it treated?

Serious "bacteremic shock" as a complication of abortion requires a well-developed fetus, fetal circulation, placenta, and a significant delay period between establishment of ovular infection and delivery. The infecting organism is usually an enterobacillus, most frequently, a hemolytic *E. coli.* The bacillus is commonly inoculated into the amniotic cavity by a foreign body used to perform a criminal abortion in the second trimester of pregnancy. Usually a deciduitis that might cause a more prompt abortion or, at least, would give early warning of the serious maternal infection is avoided. The organisms grow rapidly in the infected amniotic fluid and fetal bacteremia occurs. Fetal infection is probably through the respiratory tract. The intact, functioning fetal circulation carries the infection to the chorionic villi where the organisms multiply rapidly. The villous vessels may be completely plugged with bacteria. Meanwhile, the infection and the potent bacterial toxin, which is characteristic of these organisms, are held in check on the fetal side of the placental barrier. During this period of time, the patient may have few if any symptoms from the lethal infection that she harbors. The fetus then dies and either this development, the bacteria themselves, or the toxins produced by the bacteria destroy the placental barrier. As a result, a flood of bacteria and bacterial toxin is released suddenly into the maternal circulation from the fetal circulation. A picture of overwhelming maternal intoxication develops with dramatic suddenness. The vascular tree is that which is most seriously damaged by the toxin. Within the few hours that pass before hospitalization is accomplished, the circulating bacterial toxins have fixed in the maternal tissues. The picture of vascular collapse and lower nephron nephrosis, with oliguria or anuria, may already be established even on admission; if not, it develops rapidly. Characteristically, the patient is alert and does not show gross and significant evidence of the serious prognosis that is hers. Oliguria and hypotension may be the first signs that call attention to the correct diagnosis. Cervical smears may show that the organism is an enterococcus; blood cultures will be positive. It is essential that the uterus be emptied of the product of conception which harbors the infection and is still the primary source of the bacterial toxin. Spontaneous abortion or premature labor may help the situation and this end should be promoted by oxytocin. If spontaneous termination occurs, the uterine cavity should still be emptied of all chorionic foci by a D. and E. if and when the patient's condition permits. When vaginal delivery is impossible without delay, the question of hysterectomy is evident; opinions for and against this vary. Massive antibiotic therapy is given the mother and may be successful as far as the control of the bacteremia is concerned. The important problem, however, is to tide the patient over the critical situations caused by the bacterial toxins, which are already fixed in the maternal tissues and have resulted in severe vascular intoxication and renal shut down. An attempt to balance maternal fluids and electrolytes is made according to the usual rules governing the care of patients with renal shut down. Dialysis with an artificial kidney may be life saving. Drugs are required to maintain blood pressure when the intoxication is serious, as it usually is. Steroid therapy is included in most therapeutic routines. Any and all general supportive therapy is given. Death usually occurs from complete cardiovascular collapse, as an attempt is made to balance the fine line between blood-pressure maintenance and pulmonary edema. If the critical period of profound vascular collapse is safely passed, the problem of renal shut down may still result in a fatality.

Discuss the causes of abortion.

The fundamental causes of abortion may be classified according to their fetal, maternal, or paternal origin. In a specific case (see below) the causative factors may be multiple. Among the more common ones are:

(1) Congenitally defective germ plasm (e.g., ovular, spermatic, or the

incompatibility of their union). (2) Maternal disease: acute infection (e.g., typhoid, appendicitis) or chronic (e.g., syphilis); systemic disease (e.g., cardiac disease, endocrine dysfunction; dietary deficiency); pelvic abnormalities (fibroids, retroversion, deciduitis); poisoning (e.g., anesthetics, salicylates); emotional disturbances. (3) Trauma (criminal abortion, coitus, pelvic surgery). (4) Oxytocics. (5) Placental abnormalities (e.g., placenta praevia). (6) Abnormalities of the cord (e.g., torsion, knots).

Outline the treatment of inevitable or incomplete abortion in the first trimester of pregnancy.

The treatment has three fundamental features: evacuation of the uterus; prevention and replacement of blood loss; prevention or treatment of infection. The uterus may be emptied by oxytocics, although evacuation is more rapidly and efficiently accomplished by use of the finger, a sponge stick or placental forceps, and/or a curette. Blood loss is prevented by prompt evacuation of the uterus, by oxytocics, by intrauterine packing, or a combination of these. Blood transfusions control shock and replace blood loss. Infection can be avoided by the use of sterile techniques in all vaginal procedures, by efficient and gentle emptying of the uterus, by attention to the general health of the patient (blood transfusions), and by the prophylactic use of antimicrobial agents. Infection is combated by the same means except that vaginal or uterine manipulations, other than of the most conservative types, are contraindicated in the presence of virulent infection unless hemorrhage dictates more radical therapy. When phlebothrombosis of the pelvic veins is present, venous ligation may be indicated.

Give the diagnostic features of tubal pregnancy and its rupture.

History (see question on diagnosis of pregnancy).

Physical Examination: (1) Before rupture: normal or unilateral lower abdominal tenderness. (2) After rupture: signs of shock and intraperitoneal hemorrhage (tenderness, both direct and rebound; rigidity; diminished or absent peristalsis).

Pelvic Examination: Early but underdeveloped uterine signs of pregnancy; tender adnexal mass. In addition, after rupture: acute pelvic tenderness; signs of developing hematocele (bulging cul-de-sac or parametrial mass); aspiration of blood from the cul-de-sac.

Laboratory Data: Positive biological test for pregnancy; decidua but no ovular elements from uterine curettage; leukocytosis and increased sedimentation rate.

Review the genital changes which occur during the puerperium.

Pelvic: (1) Involution of the uterus with reduction in size and weight accompanying fatty and hyaline degeneration of the uterine muscle and connective tissue and retrogression of the vascular elements.

(2) Shedding of the decidua and regeneration of the endometrium from the connective and glandular tissue of the basalis.

(3) Healing of the placental site by regrowth of adjacent endometrium, which displaces and casts off the remaining decidua and thrombosed vessels.

(4) Healing of surgical wounds, lacerations, and contusions.

(5) Return of tone to the supportive structures of the pelvis.

(6) Return of menstruation. This occurs in 6 weeks in the absence of lactation or, not infrequently, even in the presence of nursing. The majority of nursing mothers, however, do not menstruate until lactation is completed. The first menstrual flows may or may not be of an anovulatory type.

Breasts: The onset of lactation occurs about the third or fourth postpartum day. It is preceded by breast engorgement. The stimulus for lactation is *prolactin* from the anterior pituitary.

What are after-pains?

After-pains are painful uterine contractions that are present during the first several days of the puerperium. They are more common in multipara, are normally aggravated at the time of nursing or following oxytocics, and are more severe when the uterus has been overdistended (large fetus, polyhydramnios) and after a rapid labor. They are pathologically increased by placental fragments and clots retained in the uterus. The uncomplicated type is treated by appropriate sedation.

What is lochia? Discuss its characteristics.

Lochia is the puerperal flow from the vagina. Its composition varies with the stage of involution and consists of: (1) blood, serum, debris, exudate, secretions, and bacteria from the genital tract; (2) ovular remnants.

For the first few postpartum days it is red and is rich in blood (*rubra*). As bleeding lessens and the blood is decomposed, the lochia decreases in amount and the color changes to a reddish brown (*serosa*). Finally, after the second week, there is little or no blood in the discharge and it becomes yellow or white (*alba*). The odor of the lochia may be foul due to infection. The amount, duration, and admixture of blood may be increased by infection, retained products of conception, injuries to the uterus, local pathology (i.e., fibroids), or altered physiology (i.e., endocrine disturbances or subinvolution of the placental site). The lochia may pathologically decrease or stop temporarily due to a block in the genital tract.

Discuss the management of lactation.

The conduct of lactation varies considerably. Some physicians prefer the infant to nurse for a short time at regular intervals (4 to 6 hours) before the secretion of milk has begun. Others do not have the baby suckle until the period of engorgement heralds the onset of the flow. After the secretion of milk is established, nursing is carried out on a 3- or 4-hour schedule, using alternate breasts for 20 minutes, or both breasts for 10 minutes each. The hygiene of the nipples is of the greatest importance. The nipples should be touched only after the hands have been washed. Before nursing, the areolar area is washed with water followed by boric acid, and after nursing, rinsed with sterile solution and covered with sterile gauze (dry or with a bland ointment). The infant should be kept awake during the feeding period, direct approach to the nipple simplified as much as possible, and the nasal airways kept open. A diet high in protein, vitamins, and calories is given the mother. The mother must be kept happy and comfortable because emotional upsets are frequently deleterious to the milk supply.

If fissuring of the nipples develops, it is promptly treated by one or all of the following methods: rest of the nipples (nursing only on the healthy breast, pumping, nipple shield), continued cleanliness, painting with tincture of benzoin, or the use of bland ointments.

What is constriction-ring dystocia?

An abnormality of labor in which the expulsion of the fetus is obstructed or the transmission of uterine contractions from the upper to the lower portion of the uterus is interrupted and thus cervical dilation and effacement are impeded by a circular band of contracted uterine muscle.

There are two types: (1) The pathological *ring of Bandl* occurs at the junction of the upper and lower uterine segments in the second stage of an obstructed labor. (2) A constriction ring may occur in any portion of the uterus at any time in labor and is probably due to inherent pathology in the neuromuscular conduction system of the uterus. It may be permanent or temporary.

What is a precipitate labor? What are its dangers and treatment?

Precipitate labor is one in which uterine contractions are violent, labor is short, and, as a result, delivery frequently uncontrolled. The cause of the spontaneous type is unknown. A precipitate labor may be caused by injudiciously given pituitary extract. Maternal dangers are due primarily to lacerations, but include postpartum hemorrhage owing to retained placenta or secondary uterine atony. The fetal dangers are intracranial injury, trauma from a fall, hemorrhage from a ruptured cord (the patient may be standing, unprepared for delivery), or asphyxia due to neglect (the patient may be alone and unable to care for the baby). If the obstetrician is present, treatment consists of anesthesia and control of the delivery.

Discuss the obstetric management of an Rh negative patient.

Every pregnant woman should have the Rh factor determined both because of the value of this knowledge if transfusion is necessary and also to alert the obstetrician to the possibility of erythroblastosis fetalis in the offspring. If the patient is Rh negative, past history should include questioning about previous transfusions. If previous pregnancies have occurred, signs and symptoms of erythroblastosis in the infants should be sought. The Rh of the father is essential. If he is negative, there is no problem. If he is positive, it is helpful to know if he is *heterozygous,* in which case he can sire both Rh positive and Rh negative infants, or *homozygous.* By testing the previous children of the couple one can ascertain that he is heterozygous if one of them is negative. A primigravida who has had no parenteral blood (transfusions) is not sensitized and can be assured about her first pregnancy. At the sixth month, and at intervals thereafter, the maternal blood should be checked for the presence of Rh antibodies, and, if they are present, their titer should be determined. A rising titer carries a guarded prognosis, as does one that falls late in pregnancy. The question of the value of premature delivery when antibodies exist is not answered at the time of this writing. Those who advise it base their decision on the presence of antibodies, the changes in their titer, and, at times, the history of previous erythroblastotic infants born to the mother. Another group advises against intervention on the theory that the added handicaps of prematurity counterbalance the beneficial effect derived by removing the fetus from its adverse antibody environment. To this group the problem of the potentially erythroblastotic infant is one of pediatric care: blood transfusions, oxygen therapy, and general supportive measures.

GYNECOLOGY

Define amenorrhea. How is it caused and how treated?

Amenorrhea is the absence of menstruation. *Oligomenorrhea* indicates infrequent periods. The term "hypomenorrhea" is used to indicate decreased or scant menstrual flow. Amenorrhea and its related conditions may be physiological. The years before puberty and after the menopause, and during pregnancy and lactation, are examples of physiological amenorrhea. Oligomenorrhea is frequently normal for a time after puberty and before the menopause. These conditions may be primary, that is, existent throughout the patient's earlier life, or secondary, that is, acquired. Cases of both types are multiple. Primary amenorrhea may be due to insufficiency of either or both pituitary gonadotropic hormones and ovarian hormones. Virilizing tumors may be etiological. The ovarian lesions, as is true of other endocrinopathies, may be hyper- or hypohormonal situations. A corpus-luteum retention cyst or the ovaries of Stein-Leventhal syndrome exemplify the former; congenital deficiencies, postoperative or postirradiational ovarian conditions, and postinflammatory or endometriotic ovarian lesions, the latter. Extragenital hyper- and hypohormonal situations may be etiological: hyper- or hypothyroidism; adrenal hyperplasia. Metabolic disorders may decrease or eliminate menstruation: diabetes mellitus, anorexia nervosa, chronic general disease. Psychological trauma ("hypothalamic amenorrhea") and the possibly related causes incident to environmental change are not infrequently causative. Abnormalities of the end-organs will produce these syndromes: congenital uterine hypoplasia or aplasia; tuberculous endometritis. Conditions that prevent the outflow of menstrual blood may cause apparent amenorrhea: imperforate hymen; cervical stenosis (postoperative). The menstrual disorder is only a symptom of disease rather than the disease, and the causative diseases are many and often unrelated.

Rational therapy requires, therefore, accurate diagnosis. Complete history and physical examination, including a careful pelvic examination are essential. Depending upon the findings of the fundamental work-up, numerous tests and studies may be indicated. If hormonal or metabolic disease is suspected, such diverse studies as x-ray of the sella turcica, P.B.I., blood and urinary hormonal assays, a blood sugar, to name but a few, may be required. Vaginal cytological smears and histopathological study of endometrium obtained by biopsy or D. and C. will prove helpful in evaluating the condition of the end-organs and ovarian activity. Most cases of menstrual disorders of this type that are seen in a general practice relate to the patient's general health and environment. Such cases will respond to general corrective, supportive therapy, administered intelligently and understandingly. Formal psychiatric help may be required in such situations as hypothalamic amenorrhea and anorexia nervosa. Cases of specific abnormality will require specific therapy, which may be surgical or medical. For example, tuberculous disease should be treated according to routine, established methods; cervical stenosis will require cervical dilatations; Stein-Leventhal ovaries will need wedge resection. The nonspecific "hormonal" or "functional" situations without clear-cut etiology are most difficult to treat. Good general therapy remains a cornerstone of treatment. If the patient is well and able to fulfill her childbearing wishes of the moment, no therapy save reassurance is necessary. Incidentally, many and probably most girls with hypo- or oligomenorrhea and good general health can conceive without therapy. If the situation suggests a need for regularizing or stimulating menstruation in patients of this group, cyclic hormonal therapy can be given in addition to the general therapy. This can consist of stimulation by estrogenic preparations given cyclically with expectant withdrawal-type "menstrual" bleeding 3 or 4 days after completion of several weeks' course. If circulating estrogen is normal, short courses of progesterone or one of the synthetic progestational preparations will cause withdrawal bleeding several days after completion. Pituitary or pituitary-like gonadotropins and "stimulating," small doses of roentgen therapy are still used empirically by some therapists for these patients. "Tonic" doses of thyroid or a related preparation continue to be a favorite adjunctive supplementation, and the value of this often times irrational treatment is hard to disprove.

What is dysmenorrhea? Discuss its etiology and therapy.

Dysmenorrhea is painful menstruation. A certain amount of pelvic discomfort normally and frequently precedes or accompanies the menstrual flow. If it is incapacitating, it is considered abnormal.

When dysmenorrhea has been present and relatively unchanged since early in the menstrual cycle, it is called *primary*. If the dysmenorrhea becomes more severe, or develops later in life, it is referred to as *secondary* or *acquired.*

What is "functional" or "dysfunctional" uterine bleeding? How is it treated?

The terms "functional" uterine bleeding and "dysfunctional" uterine bleeding are synonymous. They refer to cases of excessive menstruation that occur in the absence of demonstrable anatomical disease of the pelvic genital tract. The results of pelvic examination are, therefore, by definition, normal. The mechanism by which the abnormal bleeding is produced has its etiology in the function of the autonomic nervous system. The result may be mediated through the endocrine system or by direct action on the blood vessels or musculature of the uterus. Indeed, the latter mechanism may or may not be based on hormonal activity. It is probable that the hormonal changes are mediated through the pituitary gland—the local uterine changes through the musculature surrounding the terminal uterine arteries. The hormonal abnormality that is postulated is so subtle that it cannot be clearly identified by present methods used for hormonal titration. Information bearing on the etiology of this condition has been sought in the study of the normal endometrium of these cases. Other cases show an endometrial pattern of irregular ripening or irregular shedding. The smallest group, but the traditionally classic group, show endometrial hyperplasia, which is evidence of anovulatory menstruation. If the case is associated with normal endometrium and is studied carefully, one may frequently find that the endometrial response is abnormal as far as the phase of the development of the endometrium is concerned. In other words, the endometrium, although normal, is not in the phase of development that one would expect at the particular time of the cycle when the specimen was taken. Such a finding is indicative of the abnormal production of one or another of the ovarian hormones. Some cases of functional bleeding are no doubt diagnosed incorrectly. In this group, an occult cervicitis, unrecognized uterine subinvolution, a submucous myoma, or subclinical adnexal disease is the actual but unidentified cause of the menstrual problem.

The patient should be carefully and individually evaluated. General supportive measures directed at improvement of her general mental and physical health and at her enviroment are the keystone of therapy. This evaluation and treatment program is similar to that carried out in cases of amenorrhea. Severe bleeding can almost always be stopped by a D. and C. This is also the treatment of choice for patients with moderately severe functional bleeding of long standing that has responded inadequately to medical therapy. The procedure has apparent value diagnostically as well as therapeutically. Once the diagnosis has been established or in the case of single, sporadic episodes of dysfunctional bleeding, endocrine therapy can be used with benefit. Hormonal regulation of the flow is the same as that outlined for patients with amenorrhea. The value of hormonal regulation of menses for several cycles and of D. and C. is not limited to the diagnostic value and the therapeutic value of the moment. The immediate control offered by both approaches gains an interval of time for the therapist during which the abnormality is controlled. He should use this time to correct minor general problems and improve health, the foundations upon which permanent benefit must be based. Occasionally, the above therapeutic procedures fail repetitiously—and they should, at least for a time, be tried repetitiously before discarding them. Some of these cases will require hysterectomy. Every effort is made to save the uterus, however, particularly in patients of the younger age group and those who have not yet completed the family they desire. Low dosage radiation treatment to the ovaries (occasionally, to the pituitary) has been used in the past with success as far as symptom control is concerned. Either radium or deep roentgen therapy has been used. The rather recent consciousness and fear of irradiation as it relates both to the patient as a whole and to her potential childbearing ability have made this type of treatment unpopular. Its continued use must be based on the therapist's individual philosophy and the carefully individualized evaluation of each case.

How is the time of ovulation suggested or determined?

Conception proves the presence of ovulation and, in most cases in which the time of fertile intercourse is known, times it fairly accurately. It is likely that conception usually occurs within hours of fertile intercourse. The variation would be hardly more than 2 days. The egg can probably be fertilized over a period of less than 12 hours. It is unlikely for a spermatozoon to accomplish conception more than 2 days after its life work is begun. Ovulation and its timing can also be certified by culdoscopy and laparotomy. A number of presumptive tests or observations determine the time of, as well as the presence of, ovulation with some degree of accuracy:

(1) Basal temperature charts are quite accurate in certifying that ovulation occurs. The shift in temperature pattern that is the supposed criterion for timing may occur as much as several days before or after the shift or the classical "dip" that precedes the elevation.

(2) Histopathological study of an ample endometrial sample by an expert will, under normal circumstances, pinpoint the ovulatory or postovulatory day quite accurately. This test is obviously not practical for infertility work. Its accuracy is reduced when a small sample, as is often obtained by endometrial biopsy, is all that is available. Lack of normal end-organs by which to respond or supplementary hormonal therapy vitiate the results.

(3) Study of exfoliative cytology is also a job for an expert, and, in his hands, it is a valuable and practical test.

(4) Serial studies of the changes in cervical mucus can be helpful and practical. Under the influence of estrogen, the cervical mucus becomes more abundant; has a lower viscosity; develops its greatest elasticity (spinnbarkeit) and water content; becomes clearest and contains the fewest cells; and becomes most alkaline (lower limit of normal, pH 6.6). When spread on a slide, the cervical mucus, reacting to unopposed estrogenic influence, crystallizes out in an arborizing, fernlike pattern as a result of its sodium chloride content (ferning). Maximal ferning occurs at ovulation time. It is helpful in determining ovulation and the stage of the menstrual cycle, but it is a poor end point and is usually too unreliable to be practical. Its inaccuracy may increase even more if estrogen levels are low and in the presence of cervical infection. The test is helpful in evaluating a negative Sims-Huhner test by suggesting whether the poor invasion of the sperm into the cervical mucus is due to spermatic inadequacy or a defect in the cervical mucus. Spinnbarkeit, on the other hand, is less influenced by incidentals and is easily checked. This makes the use of this phenomenon one of the best, most simple, and practical tests for timing ovulation.

(5) Tests for glucose reducing agents, present with ovulation, have been popularized for determining ovulation. The chemicals necessary for the determination can be combined on a stiff piece of tape, which is inserted high against the cervix. The glucose reducing agents, indicating ovulation by their maximal concentration, react with the chemicals on the tape and give a characteristic color change to an indicator that is part of the system. Since the agents really are a part of the changes necessary for spermatic migration through the cervical mucus, this test really measures mucus acceptability rather than ovulation. If the tape is not placed so that it is bathed by cervical mucus, its value is nullified.

Infection, diabetes, and vaginitis affect the readings.

(6) A biochemical color test of Sevag and Colton measures chemicals in the urine, thought to be metabolites of follicular activity. Daily tests are employed to determine the time of ovulation.

(7) Serial hormonal titrations of the ovarian secretions and gonadotropins are also of value in pinpointing ovulation. The most widely publicized of these methods is that of Farris. In this test, daily urine specimens are inoculated into female rats. The end point, read in a relatively short time, is a color change in the rat's ovaries. The last two categories of tests are complicated for all save those "specializing" in them, and this attribute interferes with universal application. Furthermore, accuracy and/or results may not be so certain as the honest but enthusiastic investigators might believe. Such tests used for determining ovulation, as those measuring changes in electrical potential in the genital tract and certain alterations in blood platelets, are still in the experimental stage and are probably impractical for general use. Symptoms of ovulation—"mittelschmerz" and ovulatory spotting or bleeding—vary too much in their relationship to ovulation to be of important value. "Rule of thumb" methods, such as those used in calculating "rhythm calendars," are practical because they are readily accessible and easily interpreted. They are based on the fundamentals of menstrual physiology and no doubt indicate the approximate ovulatory time of the majority of average women.

How is infertility treated?

Basic to the treatment of infertility is the complete study of the infertile and the intelligence, enthusiasm, and understanding of the therapist. Study in and of itself is therapy. Abnormalities that are discovered in the investigation are corrected when the corrective measure offers sufficiently promising results. For example, elimination of infection in the male genital tract may improve the number of active sperm, improve motility, and prevent the formation of agglutinating masses of sperm, which may seriously deplete the number of available sperm. Local vaginal infection—vaginitis—should be treated appropriately. A "hostile cervical mucus" may be successfully treated by general therapeutic methods (antibiotics) or local measures (cervical fulguration or conization). A tenacious cervical mucus may be made more receptive by supplementation with small amounts of estrogens. One must avoid too high a dosage of estrogen or anovulatory cycles will result. Cervical dilatations in the office or a formal D. and C. may eliminate a hidden cervical stenosis of importance. Precoital alkaline and nutritive douches have been used to promote cervical migration. Hormonal therapy has been used to treat demonstrable deficiencies, for example, hypothyroidism, and in many empirical ways. For instance, cyclic estrogenic therapy has been used in an attempt to increase the size of a possibly hypoplastic uterus. Interestingly enough, the passage of Hegar dilators through the cervix has been suggested for the same purpose. Postovulatory progesterone is used to improve the state of the premenstrual endometrium. Ovarian hormonal therapy has been emphasized in an attempt to alter tubal motility favorably and to relieve postulated tubal spasm. Gonadotropins have been recommended to stimulate weak ovarian response. Low-dosage roentgen irradiation of the pituitary and ovaries still finds favor with some. Adrenal corticosteroid therapy has been of value in treating cases of adrenal hyperplasia. In these cases, one finds menstrual irregularity, infertility, occasionally hirsutism and acne, and elevated 17-ketosteroids. Tubal blockage may be benefited by Rubin tests and/or hysterosalpingography. Reportedly successful attempts to restore tubal patency have been reported for a technique in which cortisone, hyaluronidase, and some antibiotics have been injected in solution and under pressure into the blocked tubes, via the cervix and uterus. This technique carries overt theoretical dangers. Abdominal corrective surgery may be valuable in correcting problems incident to low-grade pelvic infection (lysis of adhesions), endometriosis, and certain cases of uterine myomas (particularly submucous tumors). Considerable effort has been expended in opening blocked tubes surgically. Some brilliant results have been forthcoming. The overall results of tuboplasty still leave a great deal to be desired. Much time and concern have been given to the general medical therapy of the patient.

Anything that will improve the general mental and physical health of the couple will improve their chances of conception. Psychotherapy of the type that can be given by the nonpsychiatrist is extremely important in many and, perhaps, most cases. One wonders how much of the success attributed to a given method of therapy should really be attributed to the significant number of spontaneous cures one encounters among infertile couples and to the enthusiasm, encouragement, and reassuring attitude developed in a good doctor-patient relationship. Hypnosis is a valuable adjunct in the treatment of a sizable group of patients, and again one wonders about the successes that might stem from the role played by suggestions that derive nonspecifically from impressive study and therapy. Anything that improves the normal response to sexual intercourse will prove beneficial in some cases. Advice about the patients' sex life is, therefore, in order. Accurate timing of intercourse with ovulation has proved helpful. Finally, one must be conscious as a therapist that his advice and course can produce functional sterility by oversensitizing a couple to their problem and perhaps by interfering with normal emotional relationships, as a result of conversation that conveys a too scientific attitude about conception.

What is a hydatid mole? Give the signs, symptoms, and treatment.

A hydatid mole is a neoplastic or degenerative disease of the fertilized ovum characterized by hydropic degeneration of the chorionic stroma, overgrowth of the trophoblastic cells, and a decrease in the stromal blood vessels of the villi. The grossly degenerated villus appears as a vesicle or grape. Extensive degeneration is incompatible with fetal development and an unknown number of fetuses are abnormal from conception (a possible cause of the hydatid degeneration); hence the fetus commonly degenerates early and is never seen.

Symptoms: Uterine bleeding, pain, and a high incidence of unusually severe toxemia are the symptoms of hydatidiform mole. *Signs* include the identification of molar tissue passed vaginally, a disproportionate increase in uterine size, absence of a demonstrable fetus, and, frequently, associated bilateral ovarian cysts (lutein cysts). *Laboratory tests* for hydatidiform mole show an extremely high titer of chorionic gonadotropic hormone demonstrable by quantitative biological methods.

Treatment: This consists of evacuation of the uterus either by dilatation and curettage or by hysterotomy. Termination of the pregnancy presents three primary dangers: hemorrhage, perforation of the uterus, and sepsis.

The postpartum care of the patient is extremely important because at least 1 or 2 per cent of moles are followed by chorionepithelioma (see next question). Prognostication of malignant transformation is made by repeated chorionic gonadotropic titrations and/or histological examination of the molar tissue. The latter is extremely difficult, and is, according to many pathologists, impossible. When malignancy is absent the gonadotropic hormone decreases and disappears, usually within several months. A continued rise in titer after the mole has been completely evacuated, or a rise after the hormonal level has been decreasing or has disappeared, is indicative of chorionepithelioma (unless another pregnancy has begun). Hormonal determinations should be repeated periodically for at least two years and at any time that suggestive symptoms reappear.

What is a chorionepithelioma? Give the signs, symptoms, and treatment.

Chorionepithelioma is a rare malignant tumor which occurs almost invariably with pregnancy or following it. Its origin is the chorionic ectoderm. The primary site is usually the uterus. Metastases to the vagina, lungs, brain, and other distant organs are common. Local spread is through the parametria. Approximately 50 per cent of the tumors follow hydatid mole; 25 per cent follow normal pregnancy; and 25 per cent follow abortion. A few cases are reported unassociated with pregnancy.

The most characteristic *symptom* is vaginal bleeding. However, metastases or spread may give the first warning of the tumor. Weight loss, weakness, and cachexia are symptoms of advanced disease. The uterus may be enlarged or normal in size. Vaginal metastasis, parametrial induration, or evidence of distant metastasis (e.g., x-ray findings of pulmonary metastasis) may be demonstrable. The presence of chorionic gonadotropic hormone gives essential confirmatory evidence (see question on hydatid mole). Uterine curettings usually reveal anaplastic trophoblastic cells showing malignant characteristics, and when the uterus is available for examination the destructive nature of the tumor is apparent.

Treatment consists of total hysterectomy and bilateral salpingo-oophorectomy. The existence of metastases is not a contraindication to surgery since they occasionally melt away. Isolated metastases may be excised. Methotrexate (4-amino-N^{10}-methyl-pteroylglutamic acid) has proved valuable in controlling metastases. Roentgen therapy is employed palliatively. The best index of cure is the persistent absence of chorionic gonadotropic hormone. Reappearance of the hormone or an increase in its titer signifies recurrence, extension, or metastasis.

Name the ulcerative lesions of the vulva. Give the laboratory tests employed for their differentiation.

Simple ulcer, chancroid, syphilis, granuloma inguinale, lymphogranuloma inguinale, tuberculosis, carcinoma.

Chancroid is diagnosed by the presence of Ducrey's bacillus in smear or culture. Darkfield examination and blood serological tests are employed to confirm the presence of syphilis. The discovery of Donovan bodies is pathognomonic for granuloma inguinale. A positive Frei test indicates the past or present existence of lymphogranuloma inguinale. Biopsy is essential for the diagnosis of carcinoma. Tuberculosis may be confirmed either by biopsy or culture. Simple ulcer is a diagnosis made by a process of elimination.

What is kraurosis vulvae? What are its symptoms and treatment?

Kraurosis vulvae is a disease of the vulva characterized by atrophy and shrinkage. The pure form of the disease shows an exaggeration of the normal senile changes in the external genitalia and must be distinguished from the similar picture of advanced leukoplakia of the vulva (see next question). The vulvar skin is thin, red, and parchment-like, and the subcutaneous tissue is atrophic. The introitus is constricted. Secondary infection is frequent.

There may be no symptoms, or *dyspareunia* may be the only complaint. Infection causes itching, pain and swelling.

Treatment is symptomatic or is directed toward the control of infection. In younger patients plastic surgical procedures may be indicated to relieve the dyspareunia. Among the therapeutic agents employed are estrogenic hormone, vitamin A, and ointments applied locally to combat infection or relieve itching.

What is leukoplakia of the vulva? Give its signs, symptoms and treatment.

Leukoplakia of the vulva is a precancerous disease. The typical skin lesion is an elevated, thickened white plaque. It may be single or multiple; it may be confined to a localized area or may involve the entire vulva and the clitoris, perineum, and perianal regions as well. The microscopic picture is characterized by hypertrophy of the epithelium, the absence of subepithelial elastic tissue, and chronic inflammation. In the advanced stage of the disease the appearance changes both grossly and microscopically to one of atrophy and shrinkage. The picture of kraurosis vulvae is duplicated but is secondary to the leukoplakia rather than primary.

Itching is the cardinal symptom, and pain is frequent. In the atrophic stage dyspareunia occurs, and secondary infection is common.

Treatment: Removal of the diseased tissue either by local excision or vulvectomy not only cures the symptoms but takes away the threat of cancer. If surgery is not employed, the leukoplakic areas must be watched because of the threat of carcinoma. Ulceration demands biopsy. At least 50 per cent of vulvar cancer follows leukoplakia. Medical therapy is the same as that employed for kraurosis vulvae except that the use of estrogens may be questioned in the presence of a potential cancer.

Discuss carcinoma of the vulva and its treatment.

Primary vulvar cancer is almost always of the epidermoid type. More than half the cases are preceded by leukoplakia of the vulva; hence itching is frequently an associated early symptom.

The presence of a lump or ulcer, pain, bloody discharge, and dysuria are among the common *symptoms.* Examination reveals a hard nodule or an ulcer, which may be papillary, friable, indurated, necrotic, and bloody. Frequently, when the patient is first seen, the inguinal lymph nodes are enlarged, either from inflammation or from cancer. The *diagnosis* is made by biopsy.

The *treatment* of choice is the Basset operation: radical vulvectomy followed, after an interval of 2 to 3 weeks, by regional lymphadenectomy (superficial and deep inguinal nodes and the femoral group). Only the patients in whom the nodes are large and fixed should be considered inoperable. Radium, radon, or x-rays to the local lesion and roentgen radiation to the metastatic areas are reserved for inoperable cases, poor surgical risks, and recurrences.

Discuss the diagnosis and treatment of vaginitis.

Vaginitis is an inflammation of the vaginal (including the cervical) skin. It is characterized by inflammation, congestion, swelling, fissuring, superficial ulceration, and oozing of the vaginal skin, producing the characteristic symptoms of increased vaginal discharge, vaginal irritation, and dyspareunia. The abundant discharge that results bathes the external genitalia and causes local swelling, redness, fissuring, and ulceration, which in turn cause itching, burning, and irritation of the skin of the external genitalia.

Vaginitis may be caused by *Trichomonas vaginalis, Candida albicans,* or nonspecific organisms. Trichomonad vaginitis is accompanied by a thin, watery, white discharge with a sweet but acrid odor. The offending organism, *Tr. vaginalis,* a parasitic, flagellate protozoon, is easily identifiable as it swims about in a warm saline hanging drop that includes a bit of secretion. Treatment consists of the daily use of a vaginal jelly or tablet which returns the abnormally alkaline vagina to a normal pH of 4.5 and usually contains an antitrichomonicide and occasionally a wetting agent. Treatment is usually prolonged to insure cure. It seems not unlikely that the vaginitis is a local sensitivity response. Based on this thesis, the addition of hydrocortisone in vaginal tablet form to the therapeutic routine may prove sound and may shorten therapy while improving the cure rate. *Tr. vaginalis* is occasionally carried by a male sex partner, and in recurrent cases this possible cause for recurrences must be investigated.

Monilial vaginitis, caused by *C. albicans,* a yeastlike fungus, is a second frequently encountered type of vaginitis. The exudate it produces is thick and white, and it often forms in plaques that adhere to the vaginal surface. The etiological organism can be cultured for diagnosis or its identity suspected in a hanging drop of sodium hydroxide containing a bit of exudate. The branching mycelia are evident beneath the microscope. This type of vaginitis is seen frequently in diabetes and pregnancy as the result of the high glycogen content of the vagina in both of these conditions. It not infrequently follows oral antibiotic therapy. Regaining or maintaining a normal vaginal pH aids in treatment or prevention of this condition. Gentian violet in liquid or jelly form is a specific. Other antifungicides, including nystatin (Mycostatin), in vaginal jelly, tablet, or douche form, have been used extensively and successfully. A typical dermatitis of the fungus type involving the skin of the external genitalia frequently accompanies the vaginitis and should be treated appropriately.

Significant degrees of nonspecific vaginitis are uncommon during adult sex life and when present usually respond to usual local hygienic measures. In prepubertal days, it may occur as the result of gonorrhea or a foreign body. The former is usually treated successfully with chemotherapeutic or antibiotic agents. The temporary transformation of the thin, unprotected, prepubertal genital epithelium to a mature vaginal skin by local or general estrogenic therapy is helpful in certain resistant cases. Local hygienic precautions after removal of the foreign body cures cases due to the latter.

Postmenopausally, and most acutely after heavy local irradiation and following acute castration, the vaginal skin atrophies and loses its protective secretions and normal pH. Vaginitis of one sort or another is frequently superimposed, with a resulting senile or atrophic vaginitis. Specific treatment as above is used if the prime offenders are the *Trichomonas* or *Candida.* Otherwise, cleansing acid douches or jellies are prescribed. Not infrequently, transformation of the atrophic skin to that of the mature sex life is required for cure and comfort. This transformation can be accomplished by estrogens used locally in a cream, jelly, or suppository preparation or by general systemic estrogenic therapy.

Discuss the treatment of upper genital-tract gonorrhea.

Acute: Penicillin and sulfadiazine in full doses are of inestimable value. Bed rest, sedation, and general supportive measures (blood transfusions, intravenous fluids, Miller-Abbott tube) are essential. Hot douches may be helpful in the subsiding stage. An abscess pointing in the posterior cul-de-sac should be drained by posterior colpotomy. If there is serious threat of rupture of an abscess, laparotomy is indicated, and, usually, the offending adnexa should be removed. The keynote of therapy is conservatism. With the advent of the antibiotic and chemotherapeutic agents, there has been a growing tendency to operate upon patients with more serious types of involvement during the early stage of their convalescence.

Chronic: A regimen of good pelvic hygiene, the removal of offending lower genital foci, attention to the patient's general health, mild sedatives and analgesics, and encouragement will frequently control or completely relieve the patient's symptoms. *Surgical intervention* is indicated for chronic incapacity that does not respond to conservative therapy—e.g., pain, menorrhagia, multiple recurring attacks, and, occasionally, tubal occlusion causing sterility. The procedure employed depends upon the type of pathology, the patient's symptoms, her age, and the desirability of retaining the childbearing function. It may vary from an operation in which only lysis of adhesions and resuspension of organs are performed to total hysterectomy with removal of both adnexa.

What are the causes of acute pelvic cellulitis? Describe the pathology.

The *beta hemolytic streptococcus* is the classical bacterial causative agent. However, many of the infections are of a mixed type and may be primarily due to a variety of organisms including other types of streptococci (both aerobic and anaerobic), staphylococci, and colonoid organisms. These bacteria, which may have been previously innocuous inhabitants of the genital tract, may be introduced at the time of infection or may spread from a remote focus in the patient.

The infection is usually precipitated by abortion (frequently criminal), by labor, or by pelvic surgery. The latter includes not only major procedures but many minor ones, such as cervical cauterization or conization and the insertion of radium or a stem pessary. Occasionally inflammation may spread without trauma from an infected, ulcerated pelvic lesion such as cancer.

The primary, acute pathological condition is a pelvic cellulitis (parametritis), perisalpingitis (contrasted with the endosalpingitis of gonorrhea), perio-ophoritis, and frequently pelvic peritonitis. The parametritis or adnexal disease may undergo suppuration and abscess formation. Since the spread is not only directly through the soft tissues, but equally through the lymphatics and blood vessels, bacteremia and phlebitis are common. These may result in distant foci of acute infection.

Discuss the etiology, symptoms, and treatment of cervicitis.

Cervical infection usually enters through and is most persistent in the endocervical glands (endocervicitis). The stroma may be involved by extension from an ulceration of the portio (erosion), but frequently the latter is secondary to an endocervicitis.

Trauma causing devitalization, fibrosis, and laceration is not only a predisposing cause, but the traumatic agent or associated manipulation may be the source of the infection. Cervicitis following delivery, abortion, or instrumentation is of this type. Stenosis of the cervical canal as the result of injury (e.g., improperly performed cauterization) or a prolapsed tumor (polyp, fibroid) may cause cervicitis. Healed lacerations may interfere with glandular drainage as well as act as poorly drained foci of infection. Specific disease such as gonorrhea is an important cause.

An abnormal discharge is the primary symptom. Relative infertility may be associated. Distant disease (e.g., arthritis, iritis) has been attributed to cervical infection. Backache or lower abdominal pain and menstrual irregularities may be due to pathological conditions that are secondary to the cervicitis (endometritis, adnexitis, parametritis).

Treatment depends upon the causative bacterial agent and the type of pathological condition. Penicillin and the chemotherapeutic agents are of value in specific diseases, such as gonorrhea and cervicitis due to certain of the streptococci. Cervical dilatation corrects stenosis and improves drainage. The removal of polyps or the cauterization of an erosion may eliminate the primary cause. Conization of the endocervix or cervical amputation excises diseased endocervical tissue and lacerations.

Name the common causes of uterine hemorrhage.

Cervical: Malignant neoplasms, benign tumors (polyp, fibroid), inflammation (erosion), laceration.

Corporeal or Fundal: Malignant neoplasms, benign tumors (polyp, fibroid, adenomyoma), complications of pregnancy (abortion, ectopic pregnancy, hydatid mole, placenta praevia, abruptio placentae), endocrine dysfunction (menopause, functional bleeding), uterine retrodisplacement, endometritis (gonorrheal), ovarian disease (postinflammatory, prolapse, granulosa-cell tumor), systemic diseases (blood dyscrasia, cardiac disease).

Discuss briefly the therapy of uterine fibroids.

The choice of treatment depends upon the patient's symptoms, the size and location of the tumor, associated pathology, the condition of the patient (including her age), and the desirability of retaining the function of childbearing.

Small tumors or even those of moderate size require no therapy other than observation if they are asymptomatic. This is particularly true when the patient is approaching the menopause, since physiological regression occurs at that time. Asymptomatic tumors associated with sterility or abortion must be carefully evaluated, because they may be coincidental rather than causative pathological changes. Myomectomy is indicated if the tumor is incriminated.

Definitive therapy is either surgical or roentgenological. The latter accomplishes its purpose by its effect on the ovaries (artificial menopause). Radiation is contraindicated if: the patient is young, childbearing is contemplated, the tumor is larger than a 3-month pregnancy, pelvic inflammatory disease is present, the diagnosis is uncertain, the symptoms are due to pressure (including unexplained pain), the tumor is submucous and of moderate size, sarcomatous transformation is suspected. Radiation therapy should always be preceded by dilatation and curettage followed by microscopic study of the curettings for neoplastic disease.

Surgery may consist of hysterectomy or myomectomy. The former is definitely curative. The latter is preferable if uterine conservation or the preservation of the childbearing function is desirable.

What are the symptoms of endometriosis and how are they produced?

Endometriosis may be asymptomatic or may produce a variety of complaints. The symptom picture depends on: (1) the cyclic distention of the endometriomas, as their endometrium grows premenstrually and bleeds within its confines at menstrual time; (2) the escape of menstrual blood as the endometriomas rupture from increasing internal pressure that results from the internal bleeding; (3) the production of adhesions from irritation caused by (2); (4) alterations in physiological function of certain pelvic organs due to (1), (2), and (3); (5) the location of endometriomas and adhesions; and (6) the severity and extent of the disease process.

As a result of (1), premenstrual or menstrual pain—acquired dysmenorrhea—in the area of involvement is the characteristic earliest symptom of endometriosis. Episodes of acute peritoneal irritation, usually at menstrual times, may occur from (2). Intermenstrual pain may be produced by (3). Dyspareunia may be the result of any or all of these developments. Tubal distortion and limitation of physiological activity may cause infertility, relative or absolute. A contribution to sterility may be made by ovarian dysfunction caused by (1), (2) and (3), and this altered ovarian function may produce menstrual irregularities. Involvement of the extragenital pelvic organs—the bowel, bladder, or ureters—may produce symptoms referrable to irritation, perforation, pressure on, and altered physiology of one or another of these organs.

What is (external) endometriosis and what signs does it produce?

Endometriosis or external endometriosis, in contrast to internal endometriosis or adenomyosis, is a disease characterized by the presence of an island or islands of endometrial tissue in areas other than the endometrial cavity of the uterus and the adjacent myometrium. These islands respond, at least when the disease is symptomatic, to the cyclic stimulus of the ovarian cycle. As a result, they produce cyclic bleeding and, since there is no normal exit for the escape of this menstrual blood, the ectopic endometrium is transformed into a blood-filled cyst, described as a chocolate cyst. The islands of ectopic endometrium may begin as viable bits of endometrium that have been transported in retrograde fashion from the uterine cavity back through the tube and into the peritoneal cavity or as the result of metaplasia of celomic epithelium. As the chocolate cysts grow with repeated episodes of bleeding, they may rupture and seed new endometriomas on adjacent peritoneal surfaces. At the same time, the irritating bloody fluid that escapes may cause significant peritoneal irritation and result in the formation of dense adhesions that involve the surfaces that have been soiled.

The signs of endometriosis are variable. Cervical stenosis, thought to be a cause for retrograde menstruation, may be demonstrated. The fundus of the uterus is not infrequently displaced to one side or the other or is adherent in the cul-de-sac, the result of secondary adhesions. The most characteristic sign of endometriosis is a relatively fine type of nodularity palpable in the cul-de-sac or the adjacent uterosacral ligaments. Firm or semicystic masses are not infrequently palpable in one or another area of the pelvis and may involve or consist of one or the other of the adnexa. As the disease progresses, these masses are invariably fixed and not infrequently tender. The masses and nodularity of endometriosis characteristically fluctuate with the menstrual cycle, becoming more prominent premenstrually and at the time of menstruation. Demonstration of this change by pelvic examinations repeated at various times in the menstrual cycle is often of great diagnostic value.

Give the international classification of cervical cancer.

The object of staging cervical cancer by criteria that are the same throughout the world has at least two advantages. It makes possible the comparisons of various methods of therapy. It gives one a background of sufficient data by which to prognosticate the possibility of cure of a patient with a tumor of given extent. The international classification is a clinical one. It is based on findings obtained by pelvic examination, by general physical examination, and by proctoscopic and cystoscopic examinations. Details of classification are still debated and, therefore, are in a state of flux. Subcategories are not listed below. The existence of definite tissue nodularity is stressed as essential evidence of paracervical spread of the tumor. A space the width of a finger must be free of nodularity in the parametrium adjacent to the pelvic wall before one can state that extension has not involved the pelvic wall. Rectal extension must be proved by biopsy. Bladder extension can be proved by biopsy. Irregularity of the bladder mucosa that is not smoothed away by digital pressure is also considered as evidence of bladder involvement. In a case in which the stage is debatable, the lower of the two possible stages is selected. The stage is determined before therapy and it is not changed thereafter: Stage 0: intraepithelial carcinoma; Stage I: the carcinoma is limited to the cervix; Stage II: the carcinoma involves the upper two thirds of the vagina and/or the parametrium, but it does not involve the pelvic wall; Stage III: the carcinoma involves the lower third of the vagina and/or the parametrium and the pelvic wall; Stage IV: the cancer involves the bladder or bowel and/or has extended beyond the confines of the pelvis.

How are cancers of the uterus diagnosed? Compare their characteristics.

There are primarily two types of uterine cancer, that of the cervix and that of the corpus. Although their symptoms are similar, their characteristics are different. Both types occur, for the most part, after the first three decades of life. The peak incidence of cervical cancer is shortly before the menopause, that of corporeal carcinoma, shortly after the menopause. Intermenstrual or postmenopausal bleeding is the most characteristic symptom of both. The first bleeding may be postcoital. Both tumors are accompanied by a purulent vaginal discharge. The discharge associated with corporeal cases, particularly in postmenopausal patients, may be intermittent and it may follow an episode of uterine cramps. These characteristics are the result of cervical blockage and the intermittent development and emptying of a pyometra. Other symptoms relate to the spread of infection or tumor into adjacent structures. Cervical cancer has the advantage of being a surface growth. It may appear as an indurated, friable, bleeding ulcer and it shows very little evidence of its extent from its surface appearance of the portio. It may present, on the other hand, as a fungating, exophytic lesion with all the typical gross characteristics of malignancy. The corporeal cancer may be accompanied by mild or moderate uterine enlargement or it may be hidden in a normal uterus. Passage of a sound into the endometrial cavity may cause unusual bleeding (Clark test) or release a pyometra. Occasionally, typically malignant tissue grows downward and protrudes out through the cervix as a polyp. Both lesions may be picked up frequently with Papanicoulaou smears. The percentage of positive smears from endometrial cancer will be increased to almost as good a percentage as that of cervical cancer if a smear is aspirated from the endometrial cavity, as well as one being taken from the surface of the vagina and cervix. The diagnosis of both tumors, whether suspected by symptoms, pelvic findings, or positive smears must await confirmation by a D. and C. and cervical biopsy and the histopathological study of the curettings and the cervical specimen.

The histological types of the tumors are usually different. The great majority of cervical cancers are epitheliomas and only about 10 per cent are adenocarcinomas. Save for an occasional adenoacanthoma or sarcoma, corporeal cancers are adenocarcinomas. Corporeal cancers seem to stay localized longer to the uterus. If we except the 10-year interval between the average ages of patients with intramucosal cervical cancer and those with invasive cervical cancers as the period of localization, this old statement does not seem justified. The spread of the two cancers is different. Cervical cancer spreads by direct extension to the paracervical tissues and the corpus. It also spreads via the lymphatics, particularly those beneath the vaginal epithelium and those of the supporting ligaments. The latter growth especially follows the cardinal ligaments, and, as a result, the groups of nodes lateral to the cervix are most frequently involved by metastasis. The subepithelial vaginal spread leads to involvement of bladder and bowel. The spread of invasive cervical cancer occurs early, but it remains localized in the pelvis for a prolonged period of time. It is detected, as is the spread of corporeal cancer, by induration—particularly, nodular induration of the tissues involved. Although the spread of corporeal cancer may be to the cervix and, from there, along the routes of the cervical spread, this is not the usual picture, at least in the average case. Corporeal cancer invades tissue directly, but it remains localized in the uterus for a rather long time in many cases. Lymphatic spread is more likely to involve the posterior groups of lymphatics, although the lateral groups that are so usually involved by cervical lesions may on occasion be involved fairly early. The characteristic posterior lymphatic spread is to the lumbar and upper hypogastric nodes and from them on upward and out of the pelvis. The external iliacs are not infrequent sites of metastasis. The localization of corporeal cancers tends to throw it in the class best suited for surgery. The lymphatic spread gives little hope that radical operation will do much more than the simple operation. Since a frequent route of metastasis is one of direct extension through the tubes and their lymphatics, and thus to the ovaries, bilateral adnexectomy is imperative.

Radiation therapy, however, may also work well. This is because the endometrial tumor does remain localized for long periods, so that massive doses of radiation can be given to the entire uterine cavity and wall by packing the cavity with radium element; and the mass radium irradiation is relatively safe because of its short penetration and the lack of fixation of vital organs around the areas containing the radiation source. Fairly good results can be expected, therefore, from radium therapy without surgery, and this second choice of treatment can be reserved for poor surgical risks and still perhaps prove adequate. When corporeal cancer has spread beyond the uterus, therapeutic results are routinely bad. The over-all 5-year salvage rate for uterine cancer is in the range of a bit more than 50 per cent. In contrast, the early spread, the type of spread, et al. of cervical cancer, does not make this tumor one that lends itself particularly to surgery. On the other hand, the prolonged localization of the tumor to the pelvis, the relative radiosensitivity of cervical cancers as a group, and an anatomical situation that makes it possible safely to attain a relatively high and often cancerocidal dosage of radiation to both the primary tumor and the regions of its metastasis, makes this tumor a particularly good one for radiation therapy.

What is the role of surgery in the treatment of malignancies of the cervix and upper genital tract?

As a rule, definitive surgical treatment of pelvic genital malignancy is radical or very radical. One type of cervical cancer and one group of ovarian tumors form occasional exceptions to this generalization. The cervical exception is intraepithelial cancer; the ovarian, the group of sex-cell tumors. Once cervical cancer has been certified as intramucosal rather than invasive, a radical conization of the cervix may be adequate therapy. All of the endocervix below the internal os, the entire cervical portio, and preferably the adjacent vaginal epithelium are excised. A moderate amount of cervical stroma underlying the epithelium is also removed. In the case of the sex-cell ovarian tumors, unilateral adnexectomy may prove sufficient if the tumor is limited grossly to the ovary. In both of these instances, the relatively conservative therapy has only one purpose—the retention of the childbearing ability. It is doubtful that these conservative operations can be justified on any other basis. The conservative approach is carried out as a calculated risk that seems worthy in individual cases. Careful, frequent, and prolonged follow-up examinations are essential if this course is taken. The cervical patient must be followed relatively frequently with Papanicoulaou vaginal smears. When childbearing is no longer a consideration, particularly in the case of the patient with the cervical lesion, one wonders whether prophylactic definitive therapy should be advised. Accepted definitive therapy of patients with intraepithelial cervical cancer is total hysterectomy. A liberal vaginal cuff should be removed with the uterus. Ovaries may be conserved. Definitive therapy for the sex-cell ovarian tumors is the same as for any other ovarian malignancy.

Surgery designed to eradicate carcinoma of the upper genital tract and the cervix can remove the following structures that may be primarily, secondarily, or potentially involved by tumor tissue: the entire uterus, including the cervix; the adnexa (the tubes and ovaries); the parametrium and paravaginal tissues (the tissues encasing the uterus and vagina); the paracervical fascia; the cardinal ligaments or bases of the broad ligaments; the pubocervical fascia, the uterosacral ligaments; the ureteral, hypogastric, iliac, inguinal, and obturator lymph channels and nodes; the bladder; the rectosigmoid, other segments of large and small intestine; and the ureters or segments of them. Unfortunately, there are certain unsatisfactory aspects of very radical pelvic surgery and their importance varies with the type of tumor and other circumstances. The first problem stems from the fact that en bloc excisions of parametrium and regional lymphatic drainage and nodes is impossible in the pelvis. Second, the important retroperitoneal lymphatic channels that drain cephalad cannot be dissected out to any satisfactory degree. Since these routes of spread are common ones for the uterus and the ovary, and since widespread intraperitoneal metastases are frequently encountered with ovarian tumors, ultraradical surgery for tumors of the corpus and ovary is probably never justified as a definitive procedure hopeful of cure. Third, radical surgery carries with it proportionately high morbidity and mortality rates unless it is done on a very rigidly chosen, ideal group of patients. Finally, and not importantly if the radical operation is the only way to cure, a colostomy and/or ureteral transplantation are frequent end results in this type of surgery. Fortunately, cancers of the uterus and ovary with the cancer limited grossly to the primary site require only total hysterectomy and bilateral salpingo-oophorectomy. Rather advanced cases of both of these tumors may be irradiated preoperatively according to individual choice. Radium is usually used in the case of uterine cancer, deep roentgen therapy for ovarian cancer. The rationale of preoperative irradiation is to seal lymphatics, reduce infection, and possibly ease an operation that might be quite difficult by shrinking the size of the original tumor. Incidentally, it is important to remove all ovarian carcinomas or cysts that may harbor carcinoma (which is every one) intact so as to prevent seeding of the peritoneal cavity and wound. Spill of uterine cancer is prevented by suturing the cervix closed before the definitive surgery begins.

The routine or classical operation for cervical cancer is the Clark-Wertheim operation. This procedure combines total hysterectomy, bilateral salpingo-oophorectomy, parametrectomy, vaginectomy, and dissection and excision of the regional lymph nodes. The Schauta operation, which is done vaginally, accomplishes the same end except that it does not include regional lymphadenectomy. Those who do these operations mistrust radiation therapy to administer a cancerocidal dose of radiation to the pelvic tissues and particularly to the cancer in the lymph nodes. They may also fear the complications of radiation therapy. On the other hand, some therapists use these operations as a second attack, that is, in cases that have proved radioresistant or have postradiation recurrence. The more radical operations that include excision of important organs or parts of them may be used with a curative attitude or a palliative one. When used with hope of cure—and this hope is limited practically to cervical cases—the surgery may be done in proved instances of radioresistance and recurrence, or it may be used with the thought that the disease is so extensive that radiation therapy will never be able to cure it and, thus, surgery is the only hope, small hope that it is. The operations can be used palliatively for any type of advanced pelvic cancer. Here the goal is to gain for the patient a bit more time, to relieve intractable pain, and/or to relieve potentially lethal obstructions of bowel or ureter in a patient who is otherwise doing well. Metastasizing ovarian cancer usually deserves exploration. At times, removal of the primary tumor, or most of it, excision of a severely involved omentum, and/or excision of a large metastatic nodule have a truly beneficial effect upon the course of the disease. Furthermore, this incomplete surgery may relieve discomfort and permit more satisfactory palliative roentgen therapy. Frequently, one of the cancerocidal chemical agents is instilled into the peritoneum at the conclusion of an operation done in this situation. This adjunct seems to reduce the rate of development of ascites in some cases, particularly in those associated with a multiplicity of tiny peritoneal transplants. Another type of surgery that is part of the routine of some therapists of cervical cancer is regional lymphadenectomy. This is done after complete radiation therapy has been accomplished. This surgery is based on the premise that cancer in lymph nodes is particularly radioresistant. Thus, care of the primary tumor and soft-tissue spread is provided by radiation and of lymph-node metastasis, by surgery.

Discuss the principles governing the radiation therapy of cervical cancer.

As a generalization, one can state that radiation therapy, expertly administered, is the treatment of choice for all cases of invasive cervical cancer. The treatment schedules vary from clinic to clinic but all combine local radium radiation with deep radiation from some distant source, usually either a high voltage roentgen therapy machine or a cobalt bomb. The object of therapy is to deliver by a combination of local and deep therapy, a cancerocidal dose of radiation to the primary tumor and its pelvic metastases, and, at the same time, to stay within a safe range of radiation dosage to the tissues through which the cancer spreads and particularly to the vital organs that surround the tumor-bearing tissue. The vital organs that must be guarded are the bladder, the rectosigmoid, the distal ureters, and the small intestine that fills the pelvis. The accomplishment of this goal requires flexibility and individualization of one's technique. Different body builds, congenital anatomical variations, and distortion caused by the growing tumor place the vital structures in varying relationships to the uterus and vagina. A relatively minor variation in the location of these structures will frequently result in over-radiation, primarily the result of the radium fraction of therapy. The radium elements deliver high doses of radiation to nearby tissues. The dose drops off rapidly, however, as distance from the radium sources increase. Different irradiation plans are encountered in different clinics. Deep roentgen radiation may be given at the onset. This therapy is directed toward the potentially lethal pelvic metastasis. Irradiation of the cervical area is avoided. Therapy is usually accomplished through multiple pelvic portals, and the full course of treatment is accomplished by daily or nearly daily treatments that deliver larger and larger dosages to a safe maximum. An average course of deep radiation therapy may require 4 to 6 weeks. Since effective radium radiation includes only the cervix and closely adjacent tissues, almost all of the total radiation dosage to the remainder of the pelvis is provided by this deep radiation. Tissue-dosage determinations are calculated throughout therapy and at its conclusion. After a variable period of time, usually a matter of a few weeks, the radium fraction of treatment may be given. This may be accomplished by one or more applications depending upon circumstances. The radium elements are usually contained in an adjustable apparatus that maintains the desired spatial distribution of the radium elements in relation to each other and in relation to the tumor and pelvic tissues. Lateral extensions press the radium well out against the bases of the broad ligaments. Usually a central stem, which may be branched, contains radium elements that will be located in the cervical canal and endometrial cavity. Other containers place radium in the pattern that is planned around and over the cervix and the primary tumor. A radium-containing mold may be used to irradiate the vagina. Some therapists use needles of varying size, containing measured amounts of radium or radon, in and around the cervix to accomplish the local irradiation. The radium containers must be firmly anchored in order to deliver with certainty, the radiation dosage that is planned. Packing is usually employed to help maintain placement and to displace the bladder and bowel as far as possible from the irradiation site. The bladder is kept empty with an indwelling catheter. X-rays should be taken to identify the radium distribution and its location in relationship to the pelvic structures. Techniques that visualize the bladder, rectosigmoid, and ureters are used simultaneously and from these films, three-dimensional spatial relationships of importance are determined. Once placed and filmed, radium dosage is calculated for the tumor, the vital structures, and the pelvic tissues that may or may not contain spreading cancer. These calculations are very complex and difficult but they are exceedingly important. Radium radiation is employed before deep x-ray therapy in some standard techniques of treatment. Whatever the details of the technique used, the combined radium and deep roentgen radiation course should be planned in advance. The preplanned, individualized technique accomplishes the theoretically most ideal therapy for the particular patient. Recalculations are made as the therapeutic plan is actually carried out and corrections and adjustments instituted so that the actual end result is as close to the theoretical, ideal plan as is possible. Using this method of therapy, only one definitive course of radiation can be given. Since maximal dosage is the goal, the tissue will not tolerate any significant amount of re-radiation. Radiation therapy that is preplanned, individualized, and carefully applied gives the best results, including the fewest complications, of any method of therapy for cervical cancer. The cure rates parallel the stages of the disease. Three quarters or more of Stage I patients should be alive and well 5 years after therapy. The rate steadily drops to the Stage IV patients, of whom only a few survive the 5-year period. Recurrences do occur between the fifth and tenth years after treatment, but these are relatively few.

What are the signs and symptoms of sarcoma of the uterus? What is the treatment?

Uterine sarcomas may be divided clinically into cervical or corporeal types, and into those that originate in fibroids and those that do not. Sarcomatous transformation of a fibroid is the more common variety and is often found by accident in the central portion of an apparently benign myoma. Localization of the sarcoma in the fibroid gives a better prognosis. Because sarcoma may be hidden in any myoma, all fibroids should be incised and grossly inspected at the operating table when conservative uterine or adnexal therapy is contemplated. The rapid growth of a fibroid suggests sarcomatous change. Other symptoms of uterine sarcoma are nonspecific: menometrorrhagia; postmenopausal bleeding; foul vaginal discharge; and the characteristic symptoms of distant metastasis or local extension.

Cervical sarcoma has the gross appearance of a malignant cervical tumor (see carcinoma). The diagnosis is made by biopsy. *Corporeal tumors* cause uterine enlargement. The latter may prolapse or extend through the cervix as a shaggy, foul, necrotic mass. Parametrial induration may be present and distant metastases may be demonstrable.

Treatment: In the absence of parametrial involvement, total hysterectomy and bilateral salpingo-oophorectomy is the treatment of choice. When the diagnosis has been made by curettage, deep x-ray therapy is of value prior to laparotomy in order to control infection. If there is demonstrable spread of the neoplasm to the pelvic cellular tissues, x-rays, radium, or their combination is preferable to surgery. Roentgen radiation is also of value in the treatment of metastatic lesions and recurrences.

What are the symptoms and signs of an ovarian neoplasm?

Symptoms: An ovarian tumor is frequently asymptomatic. As it grows, it may be palpated by the patient or cause symptoms by its weight or pressure on adjacent viscera. Pain may result from an intercurrent complication (torsion, rupture, infection, hemorrhage) or from pressure or stretching of adhesions. Menstrual irregularities are not characteristic except in certain types of tumors, i.e., granulosa-cell tumor or arrhenoblastoma.

Diagnosis: Abdominal and pelvic examinations, or, in doubtful cases, laparotomy, confirm the diagnosis. The characteristic ovarian tumor may be solid or cystic and lies in the adnexal region adjacent to the uterus. It can frequently be separated from the uterus and moved independently of it. The uteroadnexal relationship is obscured when the tumor is large or the patient difficult to examine. The differential diagnosis between an ovarian neoplasm and a non-neoplastic mass is of extreme importance. Usually the latter are less than 3 inches in diameter, their true nature is suggested by past and present history, they lie prolapsed in the pelvis, and they have a characteristic soft feel. However, differentiation may be possible only after repeated pelvic examinations which indicate the true neoplastic nature of the tumor by its persistence and growth. Other characteristics which suggest that an adnexal mass is neoplastic are: heaviness, firmness, irregularity in shape or consistency, nodularity, lobulation, papillary surface growth, the association of ascites, and an anterior position of the tumor. Rapid growth suggests malignancy.

Discuss the treatment of ovarian neoplasms.

An ovarian neoplasm should always be removed because of the dangers of malignancy, torsion, rupture, or infection, as well as to relieve symptoms caused by it. A benign tumor may be excised from its ovarian stroma or removed by salpingo-oophorectomy. All apparently benign ovarian tumors should be opened at the operating table to exclude malignancy.

Malignant ovarian lesions present a special problem. With rare exceptions (see question on functional tumors), bilateral salpingo-oophorectomy with hysterectomy is the treatment of choice. If possible, the tumor should be removed without spilling its contents into the peritoneal cavity. Radical surgery is necessary because of the frequency of microscopic metastasis to the "normal" ovary and uterus. Tumors that preoperatively appear well advanced deserve laparotomy, since occasionally even they can be removed. Also, removal of most ovarian cancers is frequently followed by improvement despite the fact that primary malignant tissue and metastatic tissue have not been completely excised. Roentgen irradiation rarely, if ever, cures ovarian cancer. However, it is of value in causing regression of tumor tissue that cannot be removed surgically, in the therapy of recurrences, and for palliation in advanced cases. Also, as the result of x-ray therapy employed preoperatively, certain of the larger, clinically inoperable tumors are reduced in size, and subsequent removal is made possible.

What are the "functional" ovarian tumors? Give their signs, symptoms and treatment.

The *feminizing neoplasms* are granulosa-cell tumor, theca-cell tumor, and luteoma. They are usually small or of moderate size. Before puberty they cause precocious sexual development including menstruation. During the active sex life there may be no characteristic symptoms, although alterations in the menstrual cycle are not uncommon. Postmenopausal bleeding is the classic symptom of the tumor developing after cessation of the menses. Because this group of tumors is malignant, the safest *therapy* is total hysterectomy and bilateral salpingo-oophorectomy. However, since the degree of malignancy is low, removal of only the involved ovary has been employed in younger patients when the other ovary was grossly normal.

The *masculinizing tumors* are the arrhenoblastoma, adrenal tumor, and masculinizing luteoma. They too are usually small or of moderate size, of low grade malignancy, and the *treatment* is the same as that of the feminizing group. Symptoms and signs are those of defeminization (cessation of menses, atrophy of the breasts, loss of characteristic female contour), followed by masculinization (hirsutism, deepening voice, hypertrophy of the clitoris).

Discuss cancer of the vagina and its treatment.

Primary cancer of the vagina is rare. Secondary carcinoma from the cervix, corpus, external genitalia, or distant organs is not uncommon.

Primary carcinoma may begin anywhere in the vagina but is most common in the proximal half of the posterior wall. It is almost always an epithelioma. There are no characteristic symptoms. Intermenstrual or postmenopausal vaginal bleeding, vaginal discharge, and, occasionally, a mass are the common symptoms. Examination reveals a firm, subepithelial nodule or a friable, papillary ulcerative lesion. The diagnosis is confirmed by biopsy. Spread is early. It is to the adjacent cellular tissues and to the regional lymph nodes (iliac, hypogastric, retroperitoneal, and, occasionally, inguinal). Retrovaginal or vesicovaginal fistula formation is a late complication.

Treatment: Although radical surgical extirpation has been attempted, the results have been poor and, at present, *radiation* therapy is the treatment of choice. The local lesion is treated with radium or radon, directly applied in filtered, molded containers or inserted into the tumor in needles. Deep roentgen therapy is directed primarily at the spread and metastases.

Discuss the surgical repair of pelvic relaxations.

The repair of any pelvic relaxation attempts to restore or substitute for the normal fascial and muscular supports. It may or may not return the pelvic organs to their normal positions.

The repair of a *urethrocele* reconstructs the torn pubocervical fascia and shortens and reapproximates the stretched urethral sphincter (urogenital diaphragm). A cystocele is corrected by an *anterior colporrhaphy* by which the pubocervical fascia is exposed and repaired. The bladder may be advanced upon the anterior surface of the uterus. *Perineorrhaphy* reapproximates the fibers of the levator ani muscle, urogenital diaphragm, and Colles' fascia. *Posterior colporrhaphy* cures a rectocele by exposing the injured rectovaginal fascia and suturing its defect over the protruding rectum. In the repair of an enterocele, the hernial sac (the posterior cul-de-sac) is dissected, its neck ligated, and the defect in the pelvic floor closed by approximating the uterosacral ligaments.

The techniques by which *uterine prolapse* is repaired are multiple. In an individual case, the choice of the procedure depends upon the associated pathology and the functional requirements. The *Manchester* or *Fothergill* operation combines anterior and posterior colporrhaphy with cervical amputation, advancement of the bladder, and shortening of the cardinal ligaments (bases of the broad ligaments). This type of procedure may be coupled with supravaginal hysterectomy, the cervical fraction being retained as a site to which the supporting tissues may be fastened. Vaginal hysterectomy removes the weight and incidental pathology of the uterus and employs the cardinal, pubocervical, and uterosacral ligaments to restore the pelvic floor. The *interposition operation* (*Watkins*) cures descensus and anterior-wall relaxation by transposing the uterus between the bladder and the pubocervical fascia. The fundus is sutured to the subsymphysial tissues. *Colpocleisis* (*Le Forte*) prevents uterine prolapse by suturing the fascia of the anterior vaginal wall to that of the posterior. Ventral fixation, a procedure with many limitations, corrects uterine descensus by suturing the fundus to the anterior abdominal wall.

Discuss the etiology, symptoms, and treatment of uterine retrodisplacement.

The uterus is held anteriorly by the uterosacral ligaments, which hold the inferior portion of the uterus posteriorly; the cardinal ligaments, which support the uterus and fix it laterally to the pelvic walls; and the round ligaments, which draw the fundus anteriorly. Intra-abdominal pressure is exerted on the posterior surface of the uterus and aids in the maintenance of the anterior position. The tone (stiffness) of the uterus is also a factor.

Retrodisplacement is favored by relaxation of the supporting ligaments (frequently as the result of childbearing) and may be contributed to by associated disease such as uterine tumors or adnexal pathology.

Symptoms: Many retrodisplaced uteri cause no symptoms. Therefore, symptoms that occur in association with retrodisplacement may not be caused by it. Among the symptoms that may be due to uterine displacement are low backache, menstrual irregularities (usually menorrhagia), pelvic discomfort (bearing-down sensation), dysmenorrhea, relative infertility, and abortion. Constipation, leukorrhea, bladder disturbances, and nervousness are among the additional symptoms that have been attributed to the condition. If symptoms can be relieved by re-placing the uterus and holding it with a pessary, there is a strong likelihood that they are due to the retrodisplacement. If this cannot be done, careful evaluation of the patient and a consideration of the other diagnostic possibilities must determine the need for uterine suspension.

Treatment: This may be either with a pessary (Smith-Hodge type) or by surgery. The latter usually employs a technique by which the round ligaments are shortened, uterosacral ligaments reefed, and, at times, the bladder advanced. Hysterectomy or, rarely, ventral fixation may be the procedures of choice if the patient has already completed her family.

Discuss the types, causes, and treatment of fistulas of the genital tract.

A fistula is an abnormal opening between two organs. In the genital tract, the following *types* are encountered: Vesicovaginal, vesicocervicovaginal, ureterovaginal, ureterocervicovaginal, urethrovaginal, rectovaginal and sigmoidovaginal. Fistulas are most commonly caused by obstructed labor, gynecological or obstetrical surgery, malignancy, or radium radiation. The *symptoms* are those of the uncontrolled passage of urine, feces, or flatus through the abnormal opening.

Treatment consists of surgical closure of the fistula or the diversion of the urinary or fecal flow (colostomy, ureteral transplantation).

Discuss the pathology, diagnosis, and treatment of genital tuberculosis.

Genital tuberculosis is almost always secondary to tuberculosis elsewhere in the body. The usual pathways to the pelvis are the blood stream or lymphatics and direct extension. The tubes are most frequently attacked and from them, or less frequently from distant foci through the vascular channels, the ovaries (perisalpingitis), uterus (endometritis), and lower genital tract (ulcerative lesion) may be involved. Tuberculous salpingitis is often associated with generalized tuberculous peritonitis. The tubal involvement may be part of a miliary blood stream spread or secondary to the peritonitis. This "wet" type is characteristically a perisalpingitis; but there may be gross parenteral involvement, and microscopic endosalpingitis is frequent.

Treatment consists of laparotomy and /or deep x-ray in small or moderate dosage. In the presence of gross parenchymatous lesions, the diseased portion may be excised. Because of the frequency of microscopic endosalpingitis, some surgeons prefer bilateral salpingo-oophorectomy if technical difficulties are not prohibitive.

Similar pathology may be associated with localized rather than generalized peritonitis. Because the genital involvement is considered primary in this type, bilateral salpingo-oophorectomy with or without hysterectomy is the surgical procedure of choice. Again, x-ray therapy may be used with, or instead of, surgery.

The "dry" or parenchymatous type of tuberculous salpingitis is difficult to distinguish from the gonorrheal form of the disease. Adhesions are denser, the tubal fimbria are more frequently open, and typical tubercles or caseation may be found. Hysterectomy with removal of the adnexa is the treatment of choice.

Frequently the diagnosis of tuberculosis of the genital tract is made for the first time at operation or even in the laboratory. Chronicity; a history or findings of tuberculosis elsewhere; signs of low grade infection (low fever, normal white count or leukopenia); decreased menstruation (frequently before the onset of pain); ascites; and the absence of history and signs of venereal disease, surgery, or pregnancy may suggest tuberculosis as the causative agent for palpable pelvic inflammatory disease.

Although only surgery and roentgen therapy have been mentioned as therapeutic measures, the general medical regimen employed in the treatment of any type of tuberculosis is equally important in the care of the patient with genital tuberculosis.

Section 10

MEDICAL JURISPRUDENCE

Describe in detail a proper medical investigation and autopsy in a case of suspected homicide.

Whenever death is found to have been caused by a fatal wound, three possibilities are present: accident, suicide, and homicide. Insist upon being given all the known facts and all the suspected conditions before arriving at any conclusion, because it is impossible from the study of the lesion alone to decide the question. Always disregard absurd theories as to the murder, lest an innocent person be convicted and executed, but never cover up a guilty person.

Inspection now calls for a study of the immediate surroundings as well as the posture of the body. If, upon inspection of the body, there are found a number of lesions as of repeated blows, stabs, or gunshot wounds, the assumption of homicidal intent will usually prove to be correct. However, it is most important to consider whether the wounds were self-inflicted or the purposeful act of another.

Examination of the body before the clothing has been removed may be of great assistance and is often very important. It is obvious that where only head injuries exist, disrobing the body will reveal nothing; however, it is safer and more thorough to remove the clothing.

Examine for location, general character, and appearance of wounds, remembering to differentiate from wounds produced by surgery.

Transmitted violence will depend on whether the part affected is able to absorb or transmit force, as well as on the nature of the adjacent organs to which such force is carried. Was it a glancing blow or did it hit squarely? It makes a difference. The effects of violence consist of:

(*a*) The mark on the surface, which may be a mere indentation or a laceration of varying kind and degree of severity.

(*b*) The deeper tissues show either indentation or lacerations with secondary effect on the inequalities of the tissues, and secondary changes that more or less quickly modify the condition of the wound.

(*c*) Transmitted effects that pass directly along the line of the blow or spread more or less diffusely or, by reason of the nature of the tissue affected, change the direction of the force altogether, as, for instance, in the case of fractures, dislocations, and sprains.

(*d*) Vascular disturbances, which are

usually marked in all extensive injuries; violent compression of the vessels may cause waves to be propagated, causing rupture at a point remote from the injury.

In gunshot wounds the kind of weapon (pistol, shotgun, rifle, machine gun) must be considered. The effect on the body will depend on the size of the projectile, its velocity, direction of flight, and the part hit. There are two kinds of powder: the old or black, and the new or smokeless. Black powder leaves a residue after combustion, and the marks differ from those left by smokeless powder.

The degree of injury inflicted, both directly and indirectly, must be determined in such a manner that one's conclusion can be presented to a body of laymen.

In performing an autopsy in such a case, unless there is something in the history to modify the plan, a general routine should be followed. After external examination of the body, which follows inspection, the chest and abdomen are opened and then the skull, if necessary. A full bladder, edema of the lungs, and congested glomeruli in the kidneys, with or without contractures of the extremities, generally point to a cerebral lesion.

Upon opening the thorax and abdomen, study the geography thoroughly and make note of the relations of the organs one to the other. Inspect the organs without handling at first. Next, be careful in handling the organs and observe the course of the wounds and the organs injured. Locate all bullets and note any and all significant things. If possible, the body should be x-rayed or at least studied with fluoroscope as an important aid in arriving at a conclusion.

Inspection with handling should include the lungs, pericardium, thoracic cavity, diaphragm, peritoneum, omentum, colon, liver, intestines, spleen, retroperitoneal structures, and pelvis.

A complete examination should be made of the heart, mediastinum, lungs, great vessels, esophagus, stomach, duodenum, pancreas, liver, intestines, kidneys, suprarenals, ureter, bladder, and sex organs. The meninges, blood vessels and various parts of the brain, the spinal cord, and the nerves are also studied.

Finally, the importance of making full and detailed notes must be emphasized, in order that an intelligent report on the autopsy findings may be made.

How would you conduct an autopsy for the purpose of testing for arsenic in the stomach, intestines, and tissues?

The cardiac and pyloric ends of the stomach and the rectal end of the intestines, or any portion desired to be removed, after being ligated in two places, just sufficiently separated to permit cutting between them, are severed, and the stomach and intestines with their contents placed *separately* into clean glass jars, hermetically sealed with some special imprint upon the seal, in such a manner that the jars cannot be opened without breaking the seal and imprint. In the same careful manner at least one kidney, the spleen, at least a portion of the liver, and the brain are removed, placed into separate clean jars, and sealed in the same manner as the stomach and intestines. Then all are properly labeled and retained until delivered to the proper official.

All appearances of each of the organs taken, abnormal or otherwise, are fully written down at the time of observation, with the assistance and corroboration of another physician, and, if possible, in the presence of the proper official.

Differentiate concussion and compression of the brain.

The *cause* of concussion is direct or indirect external force—a blow on the head, fall on the buttocks, etc. Compression may also be caused by severe external violence and, in addition, by other causes, such as abscess or tumor of the brain, intracranial hemorrhage, foreign bodies, inflammatory exudate, fracture of the skull with marked depression. Laceration of brain tissue, contusion, and compression may coexist with concussion in cases of severe injury.

In *concussion* there is momentary displacement of the brain as a whole. The centers are first stimulated, then depressed. In *compression,* owing to interference with the circulation, all the cerebral functions are impaired. The calvarium is contracted and, the brain being incompressible, the cerebrospinal fluid is displaced, the blood vessels—both arteries and veins—are compressed, and the circulation markedly impeded.

The symptoms in *concussion* come on at once and subside earlier than those of *compression,* in which the manifestations are more gradual and lasting in character.

The *course* in cases of concussion is brief and generally favorable. In compression, the duration and severity depend on the nature of the cause and its persistence. Temporary pressure, even if severe, may do no permanent harm. Recovery from moderately severe pressure is possible even after weeks of stupor. Pressure severe enough to induce coma must be relieved promptly or death will ensue.

Discuss (*a*) remote causes of death from wounds and (*b*) name at least three of said causes.

(*a*) Wounds cause death directly or indirectly. The injury is the remote cause. Death results immediately or nearly so from hemorrhage, shock, or great mechanical injury when caused by wounds directly.

Sometimes a wound that under ordinary circumstances would not be immediately fatal becomes so in consequence of some abnormal or diseased condition of the body. Other causes intervene by which death is either hastened or delayed.

(*b*) Unskilful treatment; disease; physical condition of the organs of the body.

The following are commonly found: aneurysm, an anomalous blood vessel, hernia, displacement of the viscera, osteomyelitis, blood-stream infection, old age, highly neurotic diathesis, chronic heart and kidney disease, tuberculosis, syphilis, congestion of the brain.

Differentiate cadaveric spasm from rigor mortis. Give the medicolegal significance of each.

Cadaveric spasm is that extreme condition of rigor and contraction found when the muscles have been under strong stimuli through the nerves at the time of death. *Rigor mortis,* or cadaveric rigidity, is the result of coagulation of at least part of the muscle substance and appears to begin in the plasma. The clot becomes firmer and involves other parts of the muscle substance. It comes on earlier in recently fatigued muscles. Rigor mortis comes on earlier in the smaller and more active muscles that have smaller amounts of plasma, such as those of the throat. It does not produce contraction as does cadaveric spasm, but may be associated with contraction caused by some other agent. The rate of coagulation depends on the physical and chemical conditions (especially on the latter) in fatigue stuffs and poisons. Rigor mortis follows death from any cause, while cadaveric spasm occurs under certain conditions only. Sudden or slow onset of rigor mortis is followed by similar fading. The seat of rigor mortis is the muscular system, while the seat of cadaveric spasm is the nervous system. The order of involvement in rigor mortis is: muscles of the eyes (a few minutes after death); muscles of the neck and lower jaw; chest and upper extremities; and, finally, the muscles of the abdomen and lower limbs. It usually passes off in the same order.

Immediately after death the muscles are in a state of complete relaxation and the body is pliable. This enables the examiner to say whether the person is still alive or has died recently. In death from tuberculosis or cancer, in childhood and old age, rigor mortis shows itself early and lasts but a short time. The greater the degree of muscular irritability at the time of death, as in cadaveric spasm, the later rigor mortis sets in and the longer it lasts.

The bodies of persons who have died sudden or violent deaths, apparently moved by strong emotion just prior to death; of suicides dying with the deadly weapon tightly clasped in the hand; the bodies of soldiers killed in battle develop rigor mortis without a previous period of relaxation. After death from narcotic poisons and in the body of an immature fetus, rigor mortis does not appear, or, if so, only for a short time.

How would you distinguish between antemortem and postmortem wounds?

If the signs of inflammation, swelling, and discoloration are present; if there has been exudation of pus in infected wounds or of lymph in the case of clean wounds; if suppuration, gangrene, or beginning cicatrization, either partial or permanent (recent or old), is found, such a wound may be called an antemortem wound. In the absence of these signs the wound is usually to be regarded as a postmortem wound, but the distinction is not always so clearly defined.

When a wound has caused immediate death, the above signs are missing on account of the rapid drain from the capillaries as a result of internal hemorrhage and cardiac failure. The finding of coagulated blood in a wound in a dead body is not absolute proof that the wound was inflicted before death.

Differentiate (a) molecular and somatic death. (b) Can molecular life continue after somatic death? Give an example.

(*a*) *Molecular* death is the final condition in the process of death, while *somatic* death is the death of the whole body.

(*b*) Yes. Existence of postmortem caloricity; growth of hair and nails.

What poisonous gases are given off by burning charcoal? What postmortem findings would give positive evidence that death was due to carbon oxide (monoxide) gas?

Carbon monoxide, carbon dioxide, and sulfur dioxide.

The color of skin, mucous membranes, conjunctivae, lips, all internal organs is bright red. The blood is cherry-red. The white and gray matter of the brain is reddened and on section drips cherry-red–colored blood.

There is marked asphyxia because the supply of oxygen has been cut off, the respiratory center being paralyzed by carbon monoxide gas.

What are the autopsy findings in a case of cyanide poisoning?

The dead body has a livid surface, a bloated countenance, fixed glassy eyes with dilated pupils, and clenched fingers. Sometimes, aside from excessive rigidity, it presents none of these signs.

When the body is opened, the odor of prussic acid is generally, but not always, noted.

The mouth, pharynx, and the entrance to the larynx show signs of edema and are covered with a clear, soapy, and slimy mucus, markedly acid in reaction. The stomach is usually contracted, the walls feel thick and are coated with soapy, slimy, and hemorrhagic mucus, alkaline in reaction.

Potassium cyanide is formed by the combination of cyanogen with potassium hydroxide. A solution of blood and potassium cyanide has a characteristic bright red or brownish-red color. A solution of blood and potassium hydroxide is brown or brownish black. This difference in color is seen when the stomach is examined and is important.

The important point in suspected cyanide poisoning is to be able to differentiate a case of potassium cyanide poisoning from one due to hydrocyanic acid. Even if potassium cyanide was taken, in the absence of the above-mentioned signs, we sometimes do not find any special organic changes and merely have the odor of prussic acid and the chemical studies to guide us. The reason for this is that potassium cyanide has been decomposed by the vehicle used or by the contents of the stomach, both of which were acid in reaction.

In case two people die of wounds sustained in an accident and both die about the same time, which one is assumed to be the survivor?

The severity of the wounds is the determining factor. The one who has sustained the more severe wounds is likely to have died first.

In cases of crushing injuries, or when the victims have been buried alive, as in earthquakes, which are assumed to be the survivors, children or adults, and why?

Children, because it is a question of asphyxiation, and the presumption of survivorship is in favor of children, who tolerate respiratory embarrassment longer than adults.

If one of the victims shows signs of pulmonary disease, the one with sound lungs is assumed to be the survivor.

Which bear excessive heat better, the young, the old, or the adult?

The adult tolerates heat best.

In a case of suspected drowning, how would you determine whether death had occurred from drowning or from some other cause?

To find a person dead in the water with clearly marked asphyxia is in the majority of cases conclusive evidence of drowning, but not in all.

The finding of water in the minute air passages and in the stomach suggests spasmodic attempts to breathe, which could not be produced in a dead body.

If no water is found in the air passages beyond the glottis and the latter is closed, and there is no evidence of violence, it is certain that death resulted from reflex spasm due to closure of the glottis by the irritation of the water; and if we add marked "goose flesh" plus retraction of the scrotum and, upon close examination, we find no marks of violence, then we are justified in calling it a case of drowning.

In the case of a person with apoplectic tendencies, apparently drowned, what is the presumption as to the time of death, as compared with an ordinary case of drowning?

It is presumed that death occurred earlier in such a case than in an ordinary case of asphyxiation by drowning.

State the distinction between civil and criminal malpractice.

Malpractice is careless or unskilful practice by a physician or surgeon whereby the health of the patient is impaired.

The case is one of civil malpractice when a patient brings suit for damages which he has, or thinks he has, sustained through want of skill or by reason of negligence on the part of the attending physician or surgeon.

When the state initiates the proceedings under the provisions of the criminal code, it is called "criminal malpractice."

Define "mental defective," "mental illness," "inebriate," and "criminal tendency."

Mental Defective: An individual who is not mentally ill but whose mental development is so retarded that he has not acquired enough self-control, judgment, and discretion to manage himself and his affairs, and for whose own welfare or that of others supervision, guidance, care, or control is necessary or advisable. The term includes all the grades of mental deficiency: "feebleminded," "idiot," and "imbecile."

Mental Illness: An illness which so lessens the capacity of a person to use his customary self-control, judgment, and discretion in the conduct of his affairs and social relations as to make it necessary or advisable for him to be under treatment, care, supervision, guidance, or control. The term includes lunacy, unsoundness of mind, and insanity.

Inebriate: A person is called an inebriate when he is habitually so addicted to the use of intoxicating beverages as to be unable without help, or unwilling, to stop the excessive use of such beverages. The term is synonymous with "dipsomaniac" and "habitual drunkard." Such a person is addicted to the use of alcoholic beverages and is a proper subject for restraint, care, or treatment in a hospital or prison.

Criminal Tendency: A tendency to repeat offenses against the law as shown by repeated convictions for such offenses. A tendency to habitual delinquency.

Define "delusion," "hallucination," "temporary insanity," and "lucid interval."

A *delusion* is a settled *belief* in facts that have no actual existence and that no rational person would believe.

Hallucination is a more temporary erroneous perception that may ripen into a settled belief and so become a delusion. The difference between the two is that hallucination is of a transient nature, while delusion is permanent.

Temporary insanity is the term applied to transitory periods of mental derangement preceded and followed by a sane condition of the mind.

Lucid interval is a temporary restoration to sanity of one who is insane.

Define "delusion," "systematized delusion," and "unsystematized delusion."

A *delusion* is a settled belief in facts that have no actual existence and that no rational person would believe.

Systematized delusion is defined as a delusion that so affects the subject that he can give a reason for all the assertions he makes with reference to the delusion. In such delusions the disorder has not progressed to the point of destroying the logical control of the mind over the entire range of thought, but has merely disarranged it in the region actually affected, as is the case in paranoia vera, for example.

Unsystematized delusion is the condition in which the mind of the affected individual has lost the power of systematic association of ideas and sequence of thought. Instead there is a great variety of erroneous and frequently unconnected ideas.

In order that a delusion shall constitute an excuse for an unlawful act what conditions must appear?

(1) It must appear that the act in question is the product of the delusion.

(2) The delusion must be of such a character that, if the facts were as the alleged insane person thought them to be, the act springing from the delusion would be justified.

(3) It must be of a character such as would incapacitate the defendant from distinguishing between right and wrong in a criminal matter.

What is necessary to constitute a delusion in the legal sense?

The erroneous belief must relate to material things or facts in the physical world. It may not relate to abstract questions or theories such as law, politics, or religion, since such subjects are, after all, mere matters of opinion or surmise. A delusion may or may not indicate an unsound mind, depending upon the circumstances in the case.

For the purpose of inheritance is it necessary for a child to have breathed in order to be legally "born alive"? Give accepted legal proof.

Yes. If the child's lungs are not expanded, it is stillborn even though it may have been alive as it emerged from the birth canal. Birth consists not simply in delivery but in setting up an independent existence, and this implies respiration apart from the placenta.

A child must have been born alive to the husband and wife and it must have lived with a complete and perfect respiration.

May a child conceived before marriage and born after the death of the mother yet be legitimate, although neither conceived nor born in wedlock?

Yes. Born after the death of the mother (as by cesarean section) it is held to be legitimate, although strictly speaking the marriage tie is dissolved by the death of the mother.

When mother and child die during delivery, what is the presumption as to which survived the other?

The mother survives if the child is stillborn.

The child survives if cesarean section has been performed.

This is an observation which every physician should be careful to make, as it is very important if there is property to be inherited or disposed of.

Mention two requirements which must be fulfilled for the proper disposition of property to take effect after death.

1. A properly executed will defining the final disposition of one's property.
2. The testator must be "of sound mind and memory" at the time of making the will.

"Sound mind and memory" may be defined as such a mental state as would render the testator capable of transacting the ordinary business of life.

When is it the physician's duty to prevent a patient from making a will?

When a patient is not of sound mind and memory.

What is meant by "not of sound mind and memory"?

That the maker of a will does not possess an understanding of the nature of the business in hand; that he has no recollection of (1) the property he wishes to dispose of and (2) the persons to whom he wishes to leave his property; (3) that he is incapable of designating the manner in which the property is to be divided among them.

Under what circumstances can an insane person make a valid will?

An insane person cannot make a valid will.

If, however, the person still has a disposing memory, judgment, and will which are sufficiently unclouded and free to enable him to determine (1) the nature and extent of his property and (2) the persons to whom he wishes to leave his property, and (3) if he is enjoying a lucid interval at the time of its execution, the will may be valid.

Will subsequent suicide or supervening insanity invalidate a will?

Neither will invalidate a will.

Explain the doctor's duties on the witness stand as a witness of fact and as an expert witness.

In giving evidence as to facts, a physician is called upon to testify as an ordinary witness and must confine his testimony to a statement of facts within his personal knowledge and observation; he cannot express his opinions. A physician may be examined as a medical expert only after being qualified as such. He then can express his opinions. There is a distinct difference between the two types of witness. In either case he must never become excited or facetious, nor lose his self-control from anger during a cross-examination. Above all, he must never be afraid to say "I do not know" if he really does not know the answer to the question.

Define expert testimony.

Expert testimony is the testimony rendered by a witness who, having been duly qualified, is in the discretion of the presiding judge presumed to be a person instructed by special study and possessed of special knowledge and experience of the matter at issue, concerning which he is asked to give an expert opinion. It differs from testimony given by an ordinary (lay) witness in that the latter may testify only as to facts that are observed.

Define (a) privileged communications; (b) dying declarations. (c) In what kind of cases is the latter evidence most admissible?

(*a*) *Privileged Communications:* Statements made to physicians by their patients in the course of their professional attendance upon them and necessary to enable them to prescribe for their patients or otherwise discharge their professional duties. Under the law such statements may not be testified to without the consent of the patient.

In states in which there is no statute making such communications privileged, a physician may be compelled in court to testify concerning any such communication, however confidential. In some states the law allows the physician to testify with the consent of the patient and, if the patient testifies voluntarily, the physician may be compelled to testify on the same subject. As a rule, the statutes making communications to physicians privileged do not apply in criminal cases. Such statutes have no application if such communication is for the purpose of obtaining information whereby a crime may be committed or concealed.

(*b*) *Dying Declarations:* Declarations made by a gravely injured person after all hope of recovery has been abandoned and when the said injured person believes that recovery is impossible are dying declarations. If he is actually dying but unaware of the fact, his declarations are worthless as evidence, because they are not made under oath and not in the presence of the accused. Dying declarations must be made as to facts and not opinions and are admissible only as to facts which the deceased would have been competent to testify to if living.

(*c*) *Cases of Homicide:* When the death of the victim is under investigation and the circumstances of the death are the subject of the declarations.

In some states it has been held that they are competent in the prosecution of abortion if such declarations are made competent by statute, or if causing death is a material part of the offense.

While the question of the admissibility of dying declarations is for the trial judge to decide, it is most important that the attending physician observe and record the patient's condition in order that he may by his testimony aid in the correct decision of the question.

Discuss in a general way the medicolegal and the personal responsibility of a phycian to his patient.

A physician must be qualified to practice in accordance with the statutes of the state where he resides.

Physicians are not bound to respond to every call for their services; but, having accepted a call, they must continue in attendance until recovery or other termination of the case, unless dismissed by the patient or the person employing them. They may withdraw from a case after giving reasonable notice of their intention to do so, in order that another physician may be secured.

It is not professionally ethical to contract to cure any ailment or illness.

A physician is not bound to furnish medicine without cost to his patients; he may charge for medicine and recover the value thereof.

If a surgical instrument is furnished for the patient exclusively, it may be charged to him.

If a contract is made for a physician's services for a specific time at a specific price, then so long as he continues able and willing to, and actually does, render such services in a proper manner, he cannot be legally discharged before the natural expiration of his contract. If illegally discharged, he can at the expiration of the time recover the contract price.

In order to arrive at a decision as to what is a proper charge in any given case, the position and standing of the physician and the character of services rendered should be considered, together with the financial status of the patient.

All that is necessary for the physician to show in order to recover for his services is that he has employed the ordinary degree of skill of his profession and has applied remedies fitted to the complaint and calculated to do good in general, even if the patient may have derived no benefit therefrom.

The physician is the sole judge as to the necessities of his patient and as to the number of visits required to be made.

When a surgeon is under contract with a patient to perform a certain operation, *and*, while the patient is under the anesthetic, the surgeon of his own initiative performs another and a different operation, is he liable for damages irrespective of good or bad results of said operation?

He is liable. However, most important is the wording of the written agreement or of the understanding in an oral or implied agreement when there is none in writing.

No reputable surgeon should undertake an operation without an agreement that, if he should find a condition which in his judgment necessitates removal or repairs in addition to his primary operation, he may perform any additional removal or repair operation that he believes to be to the best interest of the patient's health and comfort. In other words, he should have *carte blanche* to proceed during the operation with the understanding that he uses that degree of skill which it is the duty of every surgeon to bring to the treatment of a case.

A surgeon engages to use that skill common to the practice of surgery, not to cure, and is liable only if he fails to treat the patient skilfully.

When a surgical sponge is allowed to remain in the abdomen of a patient after a major surgical operation has been completed and the wound is almost healed, who is liable in a suit for damages for malpractice—the hospital, the operating surgeon, or the nurse in charge of the operating room? Define the status of each.

The surgeon who performed the operation, regardless of whose fault it was that the sponge was not removed (decision of the Supreme Court of Pennsylvania). Also, the nurse in charge of the operating room, if it can be established that the sponge was allowed to remain through her neglect. Charitable hospitals are exempt from liability in the State of Pennsylvania.

In a case of abortion occurring between the third and fourth months of gestation, what would lead you to suspect that it was criminally produced?

In spontaneous abortion the ovum is expelled in its entirety—i.e., the membranes are not ruptured.

A criminal abortion is usually produced by perforating the membranes, and the fetus is expelled first and the placenta and membranes afterwards.

An examination of the vagina and uterus is necessary in order to detect any marks of injury by the use of instruments. Look for wounds on the walls of the vagina and perforating wounds of the cervix and sometimes of the fundus of the uterus.

Describe the legal course you would pursue in the event of being called to a case of what you have good reason to believe is one of criminal abortion.

Establish the diagnosis by getting all the facts; examine carefully any material that may have been discharged from the uterus; examine into the cause of the abortion; call in a consultant or have the patient admitted to a hospital. If the patient dies either at home or in the hospital, write a letter to the coroner stating all the facts as you know them. It is good policy to have a consultant share the responsibility.

What attempt can be made to establish pregnancy postmortem even though disintegration of the tissue is far advanced?

The only possible criteria would be the finding of a corpus luteum in one of the ovaries and the presence of chorionic villi in the uterus. Such a diagnosis would, however, always be open to doubt.

How should a physician proceed if called into a case of rape (*a*) for the prosecution; (*b*) for the defense; (*c*) if the victim has a venereal disease?

(*a*) A complete history of every phase of the case is first obtained. The female (child or adult) is thoroughly examined, beginning with the clothing worn at the time of the alleged rape. The body generally and the genitalia are examined, for it must be determined whether penetration has occurred. Both the clothing and body must be examined for evidence of blood or semen. A microscopic examination of any vaginal discharge will show whether gonococci are present. It is important that this examination be made as soon as possible after the rape has been committed, for a delay of even a few days may mean loss of time and the actual disappearance of valuable marks of violence. These marks of violence must be distinguished from self-inflicted wounds or, quite often, from wounds purposely made by a third party for the purpose of alleging an abortion to obtain money or revenge.

(*b*) A physician for the defense must, as soon as he can, examine the boy or man. Both the clothing and body must be examined for evidence of blood or semen, and, after a careful physical examination, look for marks of violence, scratches, bruises, etc., and have a microscopic examination made of any urethral discharge to determine the presence of gonococci. A history of the case is most important because many accused are victims of the desire for money or revenge.

Some general remarks on this subject may be found of value:

Finding the hymen intact is not always proof that no rape has been committed, nor of virginity. Cases are not rare in which the hymen has to be removed after impregnation in order to permit delivery. Finding the hymen destroyed, unless the destruction is recent, does not afford positive proof of sexual intercourse.

Any degree of penetration, whether reaching the hymen or not, is sufficient to constitute the crime of rape.

There may be emission without penetration. Semen may be found in the vagina or on the genitalia.

A simple mucous vaginal discharge without signs of violence, such as contusion, lacerations, dilation of the vaginal orifice, or injury to the adjoining parts, is not conclusive proof that no rape has been committed. When vaginal discharge is mixed with blood, it is the result of violence, whereas in vaginitis it is never bloody.

The crime is so easily simulated, so hard to disprove, and so revolting, that the testimony of a careful physician may save an innocent victim from serving a term in prison.

A physician must never protect a boy or man guilty of rape.

(*c*) Microscopic examination of the vaginal discharge as well as of the urethral discharge of the accused, if there is any, is obviously indicated. The child or woman may have a gonorrheal vaginal discharge and there may be no evidence of gonorrhea in the accused.

These are vexing problems for the physician and he must proceed cautiously. The presence of a venereal disease of the same type in both parties is essential to be suggestive that rape has been committed. It must have appeared at the proper time after the alleged rape was committed.

Name four definite signs that rape has been committed.

1. Marks of violence on genitalia.
2. Marks of violence on other parts of one or both parties.
3. Spermatic or blood stains on one or both parties.

4. The presence of a venereal disease of the same type in both parties.

How do the physical findings in a case of rape on a married woman compare with the findings in the case of a child or a virgin?

In the case of a married woman the vulva and vagina may not show any signs of injury; but if the woman has made proper resistance, marks of violence will appear on the external pudenda and extensive marks of violence on her body and extremities.

A child usually offers feeble resistance, and examination of the genitalia is more likely to show marks of violence. In the case of an adult virgin both the evidences of violence on the body generally and laceration of vulva and vagina are to be expected.

How may the presence of venereal disease be relied upon as a proof of rape?

1. If both parties have the same form of the disease.

2. If the disease is sufficiently recent in the child or woman.

3. If it has made its appearance at the proper time after the alleged rape.

Under what conditions may it be possible that rape has been committed even when no evidences of lacerations or contusions can be found on the female genitalia? Why?

During the menstrual period because the parts are normally distended at this time.

Why are so many assaults, indecent assaults, attempts to ravish, rape, etc., made more frequently upon young children?

Because they are incapable of successful resistance.

A widespread belief prevails that a man suffering from a venereal disease can be cured by having sexual intercourse with a virgin.

The law states that females under a certain age are incapable of giving their consent to an act of sexual intercourse, and that such act constitutes the crime of rape. What is the age of consent? Does it vary in different states and countries?

The age of consent is:

Twelve years: Kentucky, Louisiana, Virginia, Tennessee.

Fourteen years: Alabama, Illinois, Indiana, South Carolina, Wisconsin.

Fifteen years: Texas.

Sixteen years: Arkansas, Minnesota, Montana, New York, Oregon, Pennsylvania; at sea within the maritime jurisdiction of the United States.

Eighteen years: Delaware, Colorado, Tennessee (chaste adult), Washington, Wyoming.

In England carnal knowledge of a girl under thirteen with or without consent is a felony; thirteen to sixteen years, a misdemeanor.

The belief that a girl was older than consent age is no defense.

Give the medicolegal complications that may arise when an erroneous diagnosis of pregnancy is made.

It may cast unjust suspicion on an innocent woman; may alter the terms of a will or the division of an estate; may result in a lawsuit against the physician; may result in conjugal unhappiness with divorce.

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